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(54) Title: **ANTIBACTERIAL COMPOSITIONS**

(57) Abstract: Antibacterial compositions having enhanced antibacterial effectiveness are disclosed. The antibacterial compositions contain a phenolic antibacterial agent, a surfactant or a disinfecting alcohol, and water, wherein a percent saturation of the antibacterial agent in a continuous aqueous phase of the composition is at least 25 %.

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ANTIBACTERIAL COMPOSITIONSFIELD OF THE INVENTION

5 The present invention is directed to anti-
bacterial compositions, like personal care composi-
tions, including hand sanitizer gels, having im-
proved antibacterial effectiveness. More particu-
10 larly, the present invention is directed to antibac-
terial compositions comprising an antibacterial
agent and a surfactant or a relatively low amount of
a disinfecting alcohol, and that provide a substan-
tial reduction, e.g., greater than 99%, in Gram
15 positive and Gram negative bacterial populations
within one minute.

BACKGROUND OF THE INVENTION

20 Antibacterial personal care compositions
are known in the art. Especially useful are anti-
bacterial cleansing compositions, which typically
are used to cleanse the skin and to destroy bacteria
and other microorganisms present on the skin, espe-
cially the hands, arms, and face of the user.

25 Another class of antibacterial personal
care compositions is the hand sanitizer gels. This
class of compositions is used primarily by medical
personnel to disinfect the hands and fingers. The
hand sanitizer gel is applied to, and rubbed into,
30 the hands and fingers, and the composition is al-
lowed to evaporate from the skin. Wiping of the
composition from the skin is not necessary because
the high alcohol content of present-day hand sani-

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tizer gels leads to a fast and essentially complete evaporation of the composition from the skin.

Antibacterial compositions in general are used, for example, in the health care industry, food service industry, meat processing industry, and in the private sector by individual consumers. The widespread use of antibacterial compositions indicates the importance consumers place on controlling bacteria and other microorganism populations on skin. It is important, however, that antibacterial compositions provide a substantial and broad spectrum reduction in microorganism populations quickly and without problems associated with toxicity and skin irritation.

In particular, antibacterial cleansing compositions typically contain an active antibacterial agent, a surfactant, and various other ingredients, for example, dyes, fragrances, pH adjusters, thickeners, skin conditioners, and the like, in an aqueous carrier. Several different classes of antibacterial agents have been used in antibacterial cleansing compositions. Examples of antibacterial agents include a bisguanidine (e.g., chlorhexidine digluconate), diphenyl compounds, benzyl alcohols, trihalocarbanilides, quaternary ammonium compounds, ethoxylated phenols, and phenolic compounds, such as halo-substituted phenolic compounds, like PCMX (i.e., p-chloro-m-xyleneol) and triclosan (i.e., 2,4,4'-trichloro-2'-hydroxy-diphenylether). Present-day antimicrobial compositions based on such antibacterial agents exhibit a wide range of antibacterial activity, ranging from low to high, depending

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on the microorganism to be controlled and the particular antibacterial composition.

5 Hand sanitizer gels contain a high percentage of an alcohol, like ethanol. At the high percent of alcohol present in the gel, the alcohol
10 itself acts as a disinfectant. In addition, the alcohol quickly evaporates to obviate wiping or rinsing skin treated with the sanitizer gel. Hand sanitizer gels containing a high percentage of an alcohol, i.e., about 40% or greater by weight of the composition, however, have a tendency to dry and irritate the skin.

15 Most commercial antibacterial compositions, however, generally offer a low to moderate antibacterial activity. Antibacterial activity is assessed against a broad spectrum of microorganisms, including both Gram positive and Gram negative microorganisms. The log reduction, or alternatively the percent reduction, in bacterial populations
20 provided by the antibacterial composition correlates to antibacterial activity. A log reduction of 3-5 is most preferred, a 1-3 reduction is preferred, whereas a log reduction of less than 1 is least preferred, for a particular contact time, generally
25 ranging from 15 seconds to 5 minutes. Thus, a highly preferred antibacterial composition exhibits a 3-5 log reduction against a broad spectrum of microorganisms in a short contact time. Prior disclosures illustrate attempts to provide such antibacterial compositions, which, to date, do not provide the rapid, broad range control of microorganisms desired by consumers.
30

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It should be noted that high log reductions have been achieved at pH values of 4 and 9, but such log reductions are attributed at least in part to these relatively extreme pH values. Compositions having such pH values can irritate the skin and other surfaces, and, therefore, typically are avoided. This is especially the case for hand sanitizer compositions which typically are not wiped or rinsed from the skin after use. It has been difficult to impossible to achieve a high log reduction using an antibacterial composition having a neutral pH of about 5 to about 8, and especially about 6 to about 8, without simultaneously incorporating a high percentage of an alcohol.

For example, WO 98/01110 discloses compositions comprising triclosan, surfactants, solvents, chelating agents, thickeners, buffering agents, and water. WO 98/01110 is directed to reducing skin irritation by employing a reduced amount of surfactant.

Fendler et al. U.S. 5,635,462 discloses compositions comprising PCMX and selected surfactants. The compositions disclosed therein are devoid of anionic surfactants and nonionic surfactants.

WO 97/46218 and WO 96/06152 disclose compositions based on triclosan, organic acids or salts, hydrotropes, and hydric solvents.

EP 0 505 935 discloses compositions containing PCMX in combination with nonionic and anionic surfactants, particularly nonionic block copolymer surfactants.

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WO 95/32705 discloses a mild surfactant combination that can be combined with antibacterial compounds, like triclosan.

5 WO 95/09605 discloses antibacterial compositions containing anionic surfactants and alkylpolyglycoside surfactants.

10 WO 98/55096 discloses antimicrobial wipes having a porous sheet impregnated with an antibacterial composition containing an active antimicrobial agent, an anionic surfactant, an acid, and water, wherein the composition has a pH of about 3.0 to about 6.0.

15 N.A. Allawala et al., *J. Amer. Pharm. Assoc.--Sci. Ed.*, Vol. XLII, no. 5, pp. 267-275, (1953) discusses the antibacterial activity of active antibacterial agents in combination with surfactants.

20 A.G. Mitchell, *J. Pharm. Pharmacol.*, Vol. 16, pp. 533-537, (1964) discloses compositions containing PCMX and a nonionic surfactant that exhibit antibacterial activity. The compositions disclosed in the Mitchell publication exhibit antibacterial activity in at least 47 minutes contact time, thus the compositions are not highly effective.

25 With respect to hand sanitizer gels, Osborne et al. U.S. Patent No. 5,776,430 discloses a topical antimicrobial cleaner containing chlorhexidine and an alcohol. The compositions contain about 50% to 60%, by weight, denatured alcohol and about
30 0.65 to 0.85%, by weight, chlorhexidine. The composition is applied to the skin, scrubbed into the skin, then rinsed from the skin.

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European Patent Application 0 604 848 discloses a gel-type hand disinfectant containing an antimicrobial agent, 40% to 90% by weight of an alcohol, and a polymer and a thickening agent in a combined weight of not more than 3% by weight. The gel is rubbed into the hands and allowed to evaporate to provide disinfected hands. As illustrated in EP 0 604 848, the amount and identity of the antibacterial agent is not considered important because the hand sanitizer gels contain a high percentage of an alcohol to provide antibacterial activity. The disclosed compositions often do not provide immediate sanitization and do not provide residual antibacterial efficacy.

Prior disclosures have not addressed the issue of which composition ingredient in an antibacterial composition provides bacterial control. Prior compositions also have not provided an effective, fast, and broad spectrum control of bacteria at a neutral pH of about 5 to about 8, and especially at about 6 to about 8.

An efficacious antibacterial composition has been difficult to achieve because of the properties of the antibacterial agents and the effects of a surfactant on an antibacterial agent. For example, several active antibacterial agents, like phenols, have an exceedingly low solubility in water, e.g., triclosan solubility in water is about 5 to 10 ppm (parts per million). The solubility of the antibacterial agent is increased by adding surfactants to the composition. However, an increase in solubility of the antimicrobial agent, and in turn, the amount of antibacterial agent in the composi-

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tion, does not necessarily lead to an increased antibacterial efficacy.

Without being bound to any particular theory, it is theorized that the addition of a surfactant increases antimicrobial agent solubility, but also typically reduces the availability of the antibacterial agent because a surfactant in water forms micelles above the critical micelle concentration of the surfactant. The critical micelle concentration varies from surfactant to surfactant. The formation of micelles is important because micelles have a lipophilic region that attracts and solubilizes the antibacterial agent, and thereby renders the antibacterial agent unavailable to immediately contact bacteria, and thereby control bacteria in short time period (i.e., one minute or less).

The antibacterial agent solubilized in the surfactant micelles will control bacteria, but in relatively long time frames. The antibacterial agent, if free in the aqueous solution and not tied up in the surfactant micelle (i.e., is activated), is attracted to the lipophilic membrane of the bacteria and performs its function quickly. If the antibacterial agent is tied up in the surfactant micelle (i.e., is not activated), the antibacterial agent is only slowly available and cannot perform its function in a time frame that is practical for cleaning the skin.

In addition, antibacterial agent that is solubilized in the micelle is readily washed from the skin during the rinsing process, and is not available to deposit on the skin to provide a resid-

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ual antibacterial benefit. Rather, the antibacterial agent is washed away and wasted.

5 With respect to sanitizers, hand sanitizer gels typically contain: (a) at least 60% by weight ethanol or a combination of lower alcohols, such as ethanol and isopropanol, (b) water, (c) a gelling polymer, such as a crosslinked polyacrylate material, and (d) other ingredients, such as skin conditioners, fragrances, and the like. Hand sanitizer
10 gels are used by consumers to effectively sanitize the hands, without, or after, washing with soap and water, by rubbing the hand sanitizer gel on the surface of the hands. Current commercial hand sanitizer gels rely on high levels of alcohol for
15 disinfection and evaporation, and thus suffer from disadvantages. Specifically, current hand sanitizer gels have a tendency to dry and irritate the skin because of the high levels of alcohol employed in the compositions. Also, because of the volatility
20 of ethyl alcohol, the primary active disinfectant does not remain on the skin after use, thus failing to provide a persistent, or residual, antibacterial effect.

25 At alcohol concentrations below 60%, ethyl alcohol is not recognized as an antiseptic. Thus, in compositions containing less than 60% alcohol, an additional antibacterial compound must be present to provide antibacterial activity. Prior disclosures, however, have not addressed the issue of which composition ingredient in such an antibacterial composition provides bacterial control. Therefore, for
30 formulations containing a reduced alcohol concentration, the selection of an antibacterial agent that

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provides both a rapid antibacterial effect and a persistent antibacterial benefit is difficult. Prior compositions also have not provided an effective, fast, and broad spectrum control of bacteria at a neutral pH of about 5 to about 8, and especially at about 6 to about 8.

Accordingly, a need exists for an antibacterial composition that is highly efficacious against a broad spectrum of Gram positive and Gram negative bacteria in a short time period, and wherein the antibacterial activity is attributed primarily, or solely, to the presence of the active antibacterial agent in the composition. The present invention is directed to such antibacterial compositions.

SUMMARY OF THE INVENTION

The present invention relates to antibacterial compositions that provide a substantial reduction in Gram positive and Gram negative bacteria in less than about one minute. More particularly, in one embodiment, the present invention relates to antimicrobial compositions containing an active antibacterial agent, a surfactant, and water, wherein the antibacterial agent is present in the continuous aqueous phase (in contrast to being present in micelles), in an amount of at least 50% of saturation, when measured at room temperature. The present invention also relates to antimicrobial compositions containing an active antibacterial agent, a surfactant, water, and a hydric solvent and/or a hydrotrope, wherein the antibacterial agent

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is present in an amount of at least 25% of saturation, when measured at room temperature.

5 In another embodiment, the present invention relates to antimicrobial compositions containing an active antibacterial agent, a disinfecting alcohol, a gelling agent, and water, wherein the antibacterial agent is present in an amount of at least 50% of saturation, when measured at room temperature. The present invention also relates to
10 antimicrobial compositions containing an active antibacterial agent, a disinfecting alcohol, a gelling agent, a hydrotrope, and water, wherein the antibacterial agent is present in an amount of at least 25% of saturation, when measured at room temperature.
15

Accordingly, one aspect of the present invention is to provide a liquid, antibacterial composition comprising: (a) about 0.001% to about 10%, by weight, of an antibacterial agent; (b) about
20 0.1% to about 40%, by weight, of a surfactant selected from the group consisting of a C₈-C₁₈ alkyl sulfate, a C₈-C₁₈ fatty acid salt, a C₈-C₁₈ alkyl ether sulfate having one or two moles of ethoxylation, a C₈-C₁₈ alkamine oxide, a C₈-C₁₈ alkyl sarcosinate, a
25 C₈-C₁₈ sulfoacetate, a C₈-C₁₈ sulfosuccinate, a C₈-C₁₈ alkyl diphenyl oxide disulfonate, a C₈-C₁₈ alkyl carbonate, a C₈-C₁₈ alpha-olefin sulfonate, a methyl ester sulfonate, and mixtures thereof; and (c) water, wherein the antibacterial agent is present in
30 the composition in an amount of at least 50% of saturation concentration, when measured at room temperature.

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Another aspect of the present invention is to provide an alternative embodiment of the antibacterial composition, wherein the composition comprises:

5 (a) about 0.001% to about 10%, by weight, of an antimicrobial agent;

(b) about 0.1% to about 40%, by weight, of a surfactant selected from the group consisting of an anionic surfactant, a cationic surfactant, a nonionic surfactant, an ampholytic surfactant, and mixtures thereof;

10 (c) about 0% to about 30%, by weight, of a hydrotrope;

(d) about 0% to about 25%, by weight, of a water-soluble hydric solvent; and

15 (e) water,

wherein the composition contains at least one of the hydrotrope and hydric solvent, and wherein the antimicrobial agent is present in the composition in an amount of at least 25% of saturation concentration, when measured at room temperature.

20 Still another aspect of the present invention is to provide another alternative embodiment of the antibacterial composition, wherein the composition comprises:

(a) 0.001% to about 10%, by weight, of an antimicrobial agent;

30 (b) 0 to about 10%, by weight, of a surfactant selected from the group consisting of an anionic surfactant, a cationic surfactant, a nonionic surfactant, an ampholytic surfactant, and mixtures thereof;

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(c) 0% to about 40%, by weight, of a hydrotrope;

(d) 0% to about 60%, by weight, of a water-soluble hydric solvent; and

5 (e) water,

wherein the composition contains at least one of the hydrotrope and hydric solvent in an amount sufficient to solubilize the antimicrobial agent, and wherein the antimicrobial agent is present in the composition in an amount of at least 25% of the saturation concentration, when measured at room temperature.

Another aspect of the present invention is to provide a liquid, antibacterial composition comprising: (a) about 0.05% to about 5%, by weight, of an antibacterial agent; (b) about 1% to about 40%, by weight, of a disinfecting alcohol, like a C₁₋₆ alcohol; (c) about 0.01% to about 5% by weight of a gelling agent, like a colloidal or a polymeric gelling agent; and (d) water, wherein the antibacterial agent is present in the composition in an amount of at least 50% of saturation concentration, when measured at room temperature.

Still another aspect of the present invention is to provide an alternative embodiment of the antibacterial composition, wherein the composition comprises:

(a) about 0.05% to about 5%, by weight, of an antimicrobial agent;

30 (b) about 1% to about 40%, by weight, of a disinfecting alcohol;

(c) about 0.01% to about 5%, by weight, of a gelling agent;

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(d) 0.1% to about 30%, by weight, of a hydrotrope; and

(e) water,

5 wherein the antimicrobial agent is present in the composition in an amount of at least 25% of saturation concentration, when measured at room temperature.

10 Still another aspect of the present invention is to provide another alternative embodiment of the antibacterial composition, wherein the composition comprises:

(a) 0.05% to about 5%, by weight, of an antimicrobial agent;

15 (b) about 1% to about 40%, by weight, of a disinfecting alcohol; and

(c) water,

20 wherein the composition contains the disinfecting alcohol and an optional polyhydric solvent in an amount sufficient to solubilize the antimicrobial agent, and wherein the antimicrobial agent is present in the composition in an amount of at least 25% of the saturation concentration, when measured at room temperature.

25 Yet another aspect of the present invention is to provide an antibacterial composition that exhibits a log reduction against Gram positive bacteria (i.e., *S. aureus*) of at least 2 after 30 seconds of contact.

30 Still another aspect of the present invention is to provide an antibacterial composition that exhibits a log reduction against Gram negative bacteria (i.e., *E. coli*) of at least 2.5 after 30 seconds of contact.

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Another aspect of the present invention is to provide an antibacterial composition that exhibits a substantial log reduction against Gram positive and Gram negative bacteria, and has a pH of about 5 to about 8.

Another aspect of the present invention is to provide consumer products based on an antibacterial composition of the present invention, for example, a skin cleanser, a body splash, a surgical scrub, a wound care agent, a hand sanitizer gel, a disinfectant, a mouth wash, a pet shampoo, a hard surface sanitizer, and the like.

A further aspect of the present invention is to provide a method of reducing the Gram positive and/or Gram negative bacteria populations on animal tissue, including human tissue, by contacting the tissue, like the dermis, with a composition of the present invention for a sufficient time, such as about 15 seconds to 5 minutes, to reduce the bacteria level to a desired level, and to provide a residual control of bacteria levels. The composition can be wiped or rinsed from the skin. In some embodiments, the composition is allowed to remain on the skin until the volatile components of the composition evaporate.

The above and other novel aspects and advantages of the present invention are illustrated in the following, nonlimiting detailed description of the preferred embodiments.

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DETAILED DESCRIPTION OF THE PREFERRED EMBODIMENTS

Personal care products incorporating an active antibacterial agent have been known for many years. Since the introduction of antibacterial personal care products, many claims have been made that such products provide antibacterial properties. However, to be most effective, an antibacterial composition should provide a high log reduction against a broad spectrum of organisms in as short a contact time as possible. It also would be beneficial if the antibacterial compositions provided a residual bacterial control.

As presently formulated, commercial liquid antibacterial soap compositions provide a poor to marginal time kill efficacy, i.e., rate of killing bacteria. Table 1 summarizes the kill efficacy of commercial products, each of which contains about 0.2% to 0.3%, by weight, triclosan (an antibacterial agent), and a surfactant.

Table 1 Time Kill Efficacy of Commercial Liquid Hand Soaps			
Product	Organism (Log Reductions after 1 Minute Contact Time)		
	Gram Positive <i>S. aureus</i>	Gram negative <i>E. coli</i>	Gram negative <i>K. pneum.</i>
Commercial Product A	1.39	0.00	0.04
Commercial Product B	2.20	0.00	0.01
Commercial Product C	1.85	0.00	0.00

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Antibacterial hand sanitizer compositions typically do not contain a surfactant and rely upon a high concentration of an alcohol to control bacteria. The alcohols evaporate and, therefore, cannot
5 provide residual bacterial control. The alcohols also can dry and irritate the skin.

Present-day products especially lack efficacy against Gram negative bacteria, such as *E. coli*, which are of particular concern to human
10 health. The present invention, therefore, is directed to antibacterial compositions having an exceptionally high broad spectrum antibacterial efficacy, as measured by a rapid kill of bacteria (i.e., time kill), which is to be distinguished from per-
15 sistent kill.

The present antibacterial compositions provide significantly improved time kill efficacy compared to prior compositions, for example, prior sanitizer compositions that incorporate a high per-
20 centage of an alcohol, i.e., 40% or greater, by weight. The basis of this improved time kill is the discovery that the antimicrobial efficacy of an active agent can be correlated to the rate at which the agent has access to an active site on the mi-
25 crobe. The driving force that determines the rate of agent transport to the site of action is the difference in chemical potential between the site at which the agent acts and the external aqueous phase. Alternatively stated, the microbicidal activity of
30 an active agent is proportional to its thermodynamic activity in the external phase. Accordingly, thermodynamic activity, as opposed to concentration, is the more important variable with respect to

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antimicrobial efficacy. As discussed more fully hereafter, thermodynamic activity is conveniently correlated to the percent saturation of the active antibacterial agent in the continuous aqueous phase of the composition.

Many compounds have a solubility limit in aqueous solutions termed the "saturation concentration," which varies with temperature. Above the saturation concentration, the compound precipitates from solution. Percent saturation is the measured concentration in solution divided by the saturation concentration. The concentration of a compound in aqueous solution can be increased over the saturation concentration in water by the addition of compounds like surfactants, solvents, and hydrotropes. Surfactants not only increase the solubility of compounds in the continuous aqueous phase of the composition, but also form micelles, and can solubilize compounds in the micelles.

The % saturation of an active antibacterial agent in any composition, including a surfactant-containing composition, ideally can be expressed as:

$$\% \text{ saturation} = [C/C_s] \times 100\%$$

wherein C is the concentration of antibacterial agent in the composition and C_s is the saturation concentration of the antibacterial agent in the composition at room temperature. While not wishing to be bound by any theory, applicants believe that the continuous aqueous phase of a surfactant-containing composition is in equilibrium with the micellar pseudophase of said composition, and further that any dissolved species, such as an antibac-

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terial active agent, is distributed between the aqueous continuous phase and the micellar pseudophase according to a partition law. Accordingly, the percent saturation, or alternatively the relative thermodynamic activity or relative chemical potential, of an antibacterial active agent dissolved in a composition is the same everywhere within the composition. Thus, the terms percent saturation of the antibacterial agent "in a composition," "in the aqueous continuous phase of a composition," and "in the micellar pseudophase of a composition" are interchangeable, and are used as such throughout this disclosure.

Maximum antibacterial efficacy is achieved when the difference in thermodynamic activities of the active antibacterial agent between the composition and the target organism is maximized (i.e., when the composition is more "saturated" with the active ingredient). A second factor affecting antibacterial activity is the total amount of available antibacterial agent present in the composition, which can be thought of as the "critical dose." It has been found that the total amount of active agent in the continuous aqueous phase of a composition greatly influences the time in which a desired level of antibacterial efficacy is achieved, given equal thermodynamic activities. Thus, the two key factors affecting the antibacterial efficacy of an active agent in a composition are: (1) its availability, as dictated by its thermodynamic activity, i.e., percent saturation in the continuous aqueous phase of a composition, and (2) the total amount of available active agent in the solution.

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An important ingredient in antibacterial cleansing compositions is a surfactant, which acts as a solubilizer, cleanser, and foaming agent. Surfactants affect the percent saturation of an antibacterial agent in solution, or more importantly, affect the percent saturation of the active agent in the continuous aqueous phase of the composition. This effect can be explained in the case of a sparingly water-soluble antibacterial agent in an aqueous surfactant solution, where the active agent is distributed between the aqueous (i.e., continuous) phase and the micellar pseudophase. For antibacterial agents of exceedingly low solubility in water, such as triclosan, the distribution is shifted strongly toward the micelles (i.e., a vast majority of the triclosan molecules are present in surfactant micelles, as opposed to the aqueous phase).

The ratio of surfactant to antibacterial agent directly determines the amount of active agent present in the surfactant micelles, which in turn affects the percent saturation of the active agent in the continuous aqueous phase. It has been found that as the surfactant:active agent ratio increases, the number of micelles relative to active molecules also increases, with the micelles being proportionately less saturated with active agent as the ratio increases. Since the active agent in the continuous phase is in equilibrium with active agent in the micellar pseudophase, as the saturation of antibacterial agent in the micellar phase decreases, so does the saturation of the antibacterial agent in the continuous phase. The converse is also true.

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Active agent solubilized in the micellar pseudophase is not immediately available to contact the microorganisms, and it is the percent saturation of active agent in the continuous aqueous phase that
5 determines the antibacterial activity of the composition. The active agent present in the surfactant micelles, however, can serve as a reservoir of active agent to replenish the continuous aqueous phase as the active agent is depleted.

10 To summarize, the thermodynamic activity, or percent saturation, of an antibacterial agent in the continuous aqueous phase of a composition drives antibacterial activity. Further, the total amount of available active agent determines the ultimate
15 extent of efficacy. In compositions wherein the active agent is solubilized by a surfactant, the active agent present in surfactant micelles is not directly available for antibacterial activity. For such compositions, the percent saturation of the
20 active agent in the composition, or alternatively the percent saturation of the active agent in the continuous aqueous phase of the composition, determines antibacterial efficacy.

The present compositions are antibacterial
25 compositions having an improved effectiveness against both Gram negative and Gram positive bacteria, and that exhibit a rapid bacteria kill. In one embodiment, as illustrated below, an antibacterial composition of the present invention comprises: (a)
30 about 0.001% to about 10%, by weight, of an antibacterial agent; (b) about 0.1% to about 40%, by weight, of a surfactant; (c) an optional hydric solvent; (d) an optional hydrotrope; and (e) water.

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In another embodiment, an antibacterial composition of the present invention comprises: (a) about 0.05% to about 5%, by weight, of an antibacterial agent; (b) about 1% to about 40%, by weight, of a disinfecting alcohol; (c) about 0.01% to about 5%, by weight, of a gelling agent; (d) an optional hydrotrope; and (e) water. The present compositions also can contain an optional polyhydric solvent. The compositions can further include a hydrotrope and additional optional ingredients disclosed hereafter, like polyhydric solvents, pH adjusters, dyes, skin conditioners, vitamins, and perfumes. The present compositions are free of surfactants, i.e., contain 0% to about 0.5%, by weight, of compounds that exhibit surface activity. The compositions also are mild, and provide a persistent kill because it is not necessary to rinse or wipe the compositions from the skin.

The compositions of these embodiments, and all other embodiments, have a percent saturation of antibacterial agent in the continuous aqueous phase of at least about 25%, when measured at room temperature. The compositions exhibit a log reduction against Gram positive bacteria of about 2 after 30 seconds contact. The compositions exhibit a log reduction against Gram negative bacteria of about 2.5 after 30 seconds contact.

The following illustrates important, non-limiting embodiments of the present invention.

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A. Antibacterial Compositions Containing
an Antibacterial Agent and a Surfactant

5 In one embodiment of the present invention, the antibacterial compositions comprise an active antibacterial agent, a surfactant, and water. The compositions of embodiment A exhibit a rapid
10 bacteria kill even in the absence of a hydric solvent and a hydrotrope. The presence of a hydric solvent and/or a hydrotrope does not adversely affect the antimicrobial properties of the composition, but such optional ingredients are not necessary ingredients. The compositions can further
15 include additional optional ingredients disclosed hereafter, like pH adjusters, dyes, and perfumes.

1. Antibacterial Agent

20 An antibacterial agent is present in a composition of the present invention in an amount of about 0.001% to about 10%, and preferably about 0.01% to about 5%, by weight of the composition. To achieve the full advantage of the present invention,
25 the antibacterial agent is present in an amount of about 0.05% to about 2%, by weight, of the composition.

The antibacterial compositions can be ready to use compositions, which typically contain
30 0.001% to about 2%, preferably 0.01% to about 1.5%, and most preferably about 0.05% to about 1%, of an antibacterial agent, by weight of the composition. The antibacterial compositions also can be formulated as concentrates that are diluted before use

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with one to about 100 parts water to provide an end use composition. The concentrated compositions typically contain greater than about 0.1% and up to about 10%, by weight, of the antibacterial agent.

5 Applications also are envisioned wherein the end use composition contains greater than 2%, by weight, of the antibacterial agent.

As discussed above, the absolute amount of antibacterial agent present in the composition is

10 not as important as the amount of available antibacterial agent in the composition. The amount of available antibacterial agent in the composition is related to the identity of the surfactant in the composition, the amount of surfactant in the composition, and the presence of optional ingredients in

15 the composition.

To achieve the desired bacteria kill in a short contact time, like 15 to 60 seconds, the continuous aqueous phase of the composition contains an

20 amount of antibacterial agent that is at least about 50%, and preferably at least about 75%, of the saturation concentration of the antibacterial agent in water, when measured at room temperature. To achieve the full advantage of the present invention,

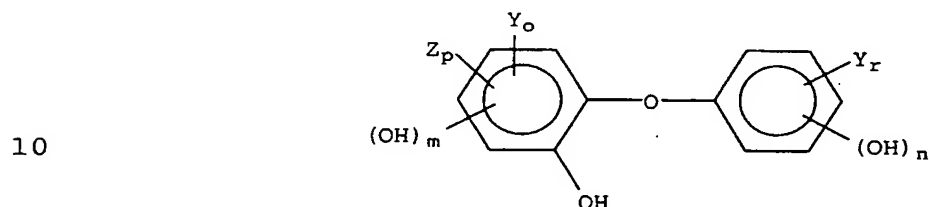
25 the continuous aqueous phase is about 95% to 100% saturated with the antibacterial agent. The amount of antibacterial agent present in the continuous aqueous phase can be defined as the total amount of antibacterial agent in the composition, less any

30 antibacterial agent present in surfactant micelles. The method of determining percent saturation of antibacterial agent in the composition is disclosed hereafter.

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The antimicrobial agents useful in the present invention are phenolic compounds exemplified by the following classes of compounds:

5 (a) 2-Hydroxydiphenyl compounds



15 wherein Y is chlorine or bromine, Z is SO₂H, NO₂, or C₁-C₄ alkyl, r is 0 to 3, o is 0 to 3, p is 0 or 1, m is 0 or 1, and n is 0 or 1.

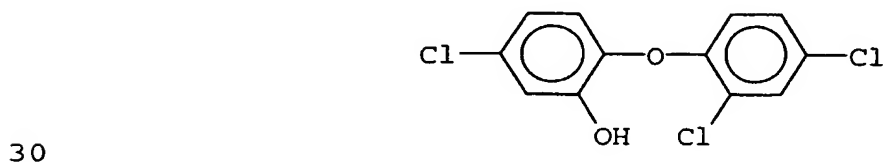
In preferred embodiments, Y is chlorine or bromine, m is 0, n is 0 or 1, o is 1 or 2, r is 1 or 2, and p is 0.

20

In especially preferred embodiments, Y is chlorine, m is 0, n is 0, o is 1, r is 2, and p is 0.

A particularly useful 2-hydroxydiphenyl compound has the structure:

25



having the adopted name, triclosan, and available commercially under the tradename IRGASAN DP300, from

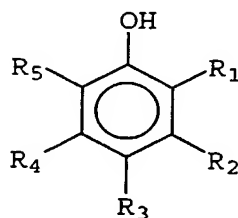
- 25 -

Ciba Specialty Chemicals Corp., Greensboro, NC.

Another useful 2-hydroxydiphenyl compound is 2,2'-dihydroxy-5,5'-dibromo-diphenyl ether.

5 (b) Phenol derivatives

10



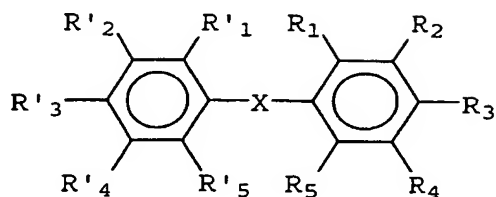
wherein R_1 is hydro, hydroxy, C_1 - C_4 alkyl, chloro, nitro, phenyl, or benzyl; R_2 is hydro, hydroxy, C_1 - C_6 alkyl, or halo; R_3 is hydro, C_1 - C_6 alkyl, hydroxy, chloro, nitro, or a sulfur in the form of an alkali metal salt or ammonium salt; R_4 is hydro or methyl, and R_5 is hydro or nitro. Halo is bromo or, preferably, chloro.

Specific examples of phenol derivatives include, but are not limited to, chlorophenols (o-, m-, p-), 2,4-dichlorophenol, p-nitrophenol, picric acid, xlenol, p-chloro-m-xlenol, cresols (o-, m-, p-), p-chloro-m-cresol, pyrocatechol, resorcinol, 4-n-hexylresorcinol, pyrogallol, phloroglucin, carvacrol, thymol, p-chlorothymol, o-phenylphenol, o-benzylphenol, p-chloro-o-benzylphenol, phenol, 4-ethylphenol, and 4-phenolsulfonic acid. Other phenol derivatives are listed in WO 98/55096, incorporated herein by reference.

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(c) Diphenyl Compounds

5



10 wherein X is sulfur or a methylene group, R_1 and R'_1 are hydroxy, and R_2 , R'_2 , R_3 , R'_3 , R_4 , R'_4 , R_5 , and R'_5 , independent of one another, are hydro or halo. Specific, nonlimiting examples of diphenyl compounds are hexachlorophene, tetrachlorophene, dichloro-
 15 phene, 2,3-dihydroxy-5,5'-dichlorodiphenyl sulfide, 2,2'-dihydroxy-3,3',5,5'-tetrachlorodiphenyl sulfide, 2,2'-dihydroxy-3,5',5,5',6,6'-hexachlorodiphenyl sulfide, and 3,3'-dibromo-5,5'-dichloro-2,2'-dihydroxydiphenylamine. Other diphenyl compounds
 20 are listed in WO 98/55096, incorporated herein by reference.

2. Surfactant

25

In addition to the antibacterial agent, a present antimicrobial composition also contains a surfactant. The surfactant is present in an amount of about 0.1% to about 40%, and preferably about 0.3% to about 20%, by weight, of the composition.
 30 To achieve the full advantage of the present invention, the antibacterial composition contains about 0.5% to about 15%, by weight, of the surfactant.

- 27 -

Ready-to-use compositions typically contain about 0.1% to about 10%, preferably about 0.3% to about 5%, and most preferably, 0.5% to about 3%, by weight, of the composition. Concentrated compositions suitable for dilution typically contain
5 greater than about 5%, by weight, of a surfactant.

The amount of surfactant present in the composition is related to the amount and identity of the antibacterial agent in the composition and to
10 the identity of the surfactant. The amount of surfactant is determined such that the percent saturation of the antibacterial agent in the continuous aqueous phase of the composition is at least about 50%, preferably at least about 75%, and most preferably
15 at least about 95%.

In this embodiment, wherein the presence of a hydric solvent and a hydrotrope is optional, the identity of the surfactant is important with respect to providing a composition having a percent
20 saturation of antibacterial agent in the continuous aqueous phase of at least about 50%. As illustrated hereafter, surfactants useful in this embodiment of the invention include anionic surfactants and selected cationic surfactants. Nonionic surfactants
25 and anionic surfactants containing a relatively high amount of ethoxylation are not useful in this embodiment. Ethoxylated surfactants containing more than two moles of ethylene oxide have a strong affinity for the antibacterial agent, and in this
30 embodiment substantially reduce the efficacy of the antibacterial agent.

Accordingly, in this embodiment, the surfactant is selected from the following classes of

- 28 -

surfactants: a C₈-C₁₈ alkyl sulfate, a C₈-C₁₈ fatty acid salt, a C₈-C₁₈ alkyl ether sulfate having one or two moles of ethoxylation, a C₈-C₁₈ alkamine oxide, a C₈-C₁₈ alkoyl sarcosinate, a C₈-C₁₈ sulfoacetate, a C₈-C₁₈ sulfosuccinate, a C₈-C₁₈ alkyl diphenyl oxide disulfonate, a C₈-C₁₈ alkyl carbonate, a C₈-C₁₈ alpha-olefin sulfonate, a methyl ester sulfonate, and mixtures thereof. The C₈-C₁₈ alkyl group contains eight to sixteen carbon atoms, and can be straight chain (e.g., lauryl) or branched (e.g., 2-ethylhexyl). The cation of the anionic surfactant can be an alkali metal (preferably sodium or potassium), ammonium, C₁-C₄ alkylammonium (mono-, di-, tri), or C₁-C₃ alkanolammonium (mono-, di-, tri-). Lithium and alkaline earth cations (e.g., magnesium) can be used, but antibacterial efficacy is reduced.

Specific surfactants that can be used in this embodiment include, but are not limited to, lauryl sulfates, octyl sulfates, 2-ethylhexyl sulfates, lauramine oxide, decyl sulfates, tridecyl sulfates, cocoates, lauroyl sarcosinates, lauryl sulfosuccinates, linear C₁₀ diphenyl oxide disulfonates, lauryl sulfosuccinates, lauryl ether sulfates (1 and 2 moles ethylene oxide), myristyl sulfates, oleates, stearates, tallates, cocamine oxide, decylamine oxide, myristamine oxide, ricinoleates, cetyl sulfates, and similar surfactants. Additional examples of surfactants can be found in "CTFA Cosmetic Ingredient Handbook," J.M. Nikitakis, ed., The Cosmetic, Toiletry and Fragrance Association, Inc., Washington, D.C. (1988) (hereafter CTFA Handbook), pages 10-13, 42-46, and 87-94, incorporated herein by reference.

- 29 -

3. Carrier

The carrier in this embodiment comprises water.

5

4. Optional Ingredients

An antibacterial composition of the present invention also can contain optional ingredients well known to persons skilled in the art. For example, the composition can contain a hydric solvent and/or a hydrotrope. These particular optional ingredients and the amount that can be present in the composition are discussed hereafter.

The compositions also can contain other optional ingredients, such as dyes and fragrances, that are present in a sufficient amount to perform their intended function and do not adversely affect the antibacterial efficacy of the composition. Such optional ingredients typically are present, individually, from 0% to about 5%, by weight, of the composition, and, collectively, from 0% to about 20%, by weight, of the composition.

Classes of optional ingredients include, but are not limited to, dyes, fragrances, pH adjusters, thickeners, viscosity modifiers, buffering agents, foam stabilizers, antioxidants, foam enhancers, chelating agents, opacifiers, and similar classes of optional ingredients known to persons skilled in the art.

Specific classes of optional ingredients include alkanolamides as foam boosters and stabilizers; gums and polymers as thickening agents; inor-

- 30 -

ganic phosphates, sulfates, and carbonates as buffering agents; EDTA and phosphates as chelating agents; and acids and bases as pH adjusters.

5 Examples of preferred classes of basic pH adjusters are ammonia; mono-, di-, and tri-alkyl amines; mono-, di-, and tri-alkanolamines; alkali metal and alkaline earth metal hydroxides; and mixtures thereof. However, the identity of the basic pH adjuster is not limited, and any basic pH ad-
10 juster known in the art can be used. Specific, nonlimiting examples of basic pH adjusters are ammonia; sodium, potassium, and lithium hydroxide; monoethanolamine; triethylamine; isopropanolamine; diethanolamine; and triethanolamine.

15 Examples of preferred classes of acidic pH adjusters are the mineral acids and polycarboxylic acids. Nonlimiting examples of mineral acids are hydrochloric acid, nitric acid, phosphoric acid, and sulfuric acid. Nonlimiting examples of polycar-
20 boxylic acids are citric acid, glycolic acid, and lactic acid. The identity of the acidic pH adjuster is not limited and any acidic pH adjuster known in the art, alone or in combination, can be used.

 An alkanolamide to provide composition
25 thickening, foam enhancement, and foam stability can be, but are not limited to, cocamide MEA, cocamide DEA, soyamide DEA, lauramide DEA, oleamide MIPA, stearamide MEA, myristamide MEA, lauramide MEA, capramide DEA, ricinoleamide DEA, myristamide DEA,
30 stearamide DEA, oleylamide DEA, tallowamide DEA, lauramide MIPA, tallowamide MEA, isostearamide DEA, isostearamide MEA, and mixtures thereof.

- 31 -

B. Antibacterial Compositions Containing
an Antibacterial Agent, a Surfactant,
and a Hydric Solvent and/or a Hydrotrope

5

In another embodiment, the antibacterial compositions comprise an active antibacterial agent, a surfactant, and a hydric solvent and/or a hydro-trope. The compositions of embodiment B exhibit a rapid bacteria kill, and are essentially unlimited in the identity of the surfactant in the composition. The solvent and/or hydrotrope assists in solubilizing the antibacterial agent, and reduces the affinity of the antibacterial agent to enter surfactant micelles. Accordingly, at least 25% saturation of the antibacterial agent in the continuous aqueous phase can be achieved regardless of the identity of the surfactant.

20

1. Antibacterial Agent

The amount and identity of the antibacterial agent present in this embodiment of the invention is discussed above in A.1.

25

In addition, to achieve the desired bacteria kill in a short contact time, like 15 to 60 seconds, the continuous aqueous phase of the composition contains an amount of antibacterial agent that is at least about 25%, and preferably at least about 50, and more preferably at least about 75%, of the saturation concentration of the antibacterial agent in water, when measured at room temperature. To achieve the full advantage of the present inven-

30

- 32 -

tion, the continuous aqueous phase is about 95% to 100% saturated with the antibacterial agent.

2. Surfactant

5

The amount of surfactant present in this embodiment of the present invention is identical to the amount disclosed above in A.2. However, due to the presence of a hydric solvent and/or a hydro-
10 trope, the identity of the surfactant is not limited as in A.2.

In particular, the presence of a hydric solvent and/or hydrotrope, as defined hereafter, reduces the affinity of the antibacterial agent to enter surfactant micelles. Accordingly, a suffi-
15 cient amount of the antibacterial agent is present in the continuous aqueous phase to quickly and effectively kill a broad spectrum of bacteria regardless of the identity of the surfactant. In embodi-
20 ments wherein a hydric solvent and hydrotrope are absent, various surfactants, like ethoxylated nonionic surfactants, have such a strong affinity for the antibacterial agent that the antibacterial agent is not available for a rapid bacteria kill.

25 Accordingly, in this embodiment the surfactant can be an anionic surfactant, a cationic surfactant, a nonionic surfactant, or a compatible mixture of surfactants. The surfactant also can be an ampholytic or amphoteric surfactant, which have
30 anionic or cationic properties depending upon the pH of the composition.

The antibacterial compositions, therefore, can contain an anionic surfactant disclosed above in

- 33 -

A.2., and more generally can contain any anionic surfactant having a hydrophobic moiety, such as a carbon chain including about 8 to about 30 carbon atoms, and particularly about 12 to about 20 carbon atoms, and further has a hydrophilic moiety, such as sulfate, sulfonate, carbonate, phosphate, or carboxylate. Often, the hydrophobic carbon chain is etherified, such as with ethylene oxide or propylene oxide, to impart a particular physical property, such as increased water solubility or reduced surface tension to the anionic surfactant.

Therefore, suitable anionic surfactants include, but are not limited to, compounds in the classes known as alkyl sulfates, alkyl ether sulfates, alkyl ether sulfonates, sulfate esters of an alkylphenoxy polyoxyethylene ethanol, alpha-olefin sulfonates, beta-alkoxy alkane sulfonates, alkylaryl sulfonates, alkyl monoglyceride sulfates, alkyl monoglyceride sulfonates, alkyl carbonates, alkyl ether carboxylates, fatty acids, sulfosuccinates, sarcosinates, oxtoxynol or nonoxynol phosphates, taurates, fatty taurides, fatty acid amide polyoxyethylene sulfates, isethionates, or mixtures thereof. Additional anionic surfactants are listed in McCutcheon's Emulsifiers and Detergents, 1993 Annuals, (hereafter McCutcheon's), McCutcheon Division, MC Publishing Co., Glen Rock, NJ, pp. 263-266, incorporated herein by reference. Numerous other anionic surfactants, and classes of anionic surfactants, are disclosed in Laughlin et al. U.S. Patent No. 3,929,678, incorporated herein by reference.

The antibacterial compositions also can contain nonionic surfactants. Typically, a nonionic

- 34 -

surfactant has a hydrophobic base, such as a long chain alkyl group or an alkylated aryl group, and a hydrophilic chain comprising a sufficient number (i.e., 1 to about 30) of ethoxy and/or propoxy moieties. Examples of classes of nonionic surfactants include ethoxylated alkylphenols, ethoxylated and propoxylated fatty alcohols, polyethylene glycol ethers of methyl glucose, polyethylene glycol ethers of sorbitol, ethylene oxide-propylene oxide block copolymers, ethoxylated esters of fatty (C_8 - C_{18}) acids, condensation products of ethylene oxide with long chain amines or amides, and mixtures thereof.

Exemplary nonionic surfactants include, but are not limited to, methyl gluceth-10, PEG-20 methyl glucose distearate, PEG-20 methyl glucose sesquistearate, C_{11-15} pareth-20, ceteth-8, ceteth-12, dodoxynol-12, laureth-15, PEG-20 castor oil, poly-sorbate 20, steareth-20, polyoxyethylene-10 cetyl ether, polyoxyethylene-10 stearyl ether, polyoxyethylene-20 cetyl ether, polyoxyethylene-10 oleyl ether, polyoxyethylene-20 oleyl ether, an ethoxylated nonylphenol, ethoxylated octylphenol, ethoxylated dodecylphenol, or ethoxylated fatty (C_6 - C_{22}) alcohol, including 3 to 20 ethylene oxide moieties, polyoxyethylene-20 isohexadecyl ether, polyoxyethylene-23 glycerol laurate, polyoxy-ethylene-20 glyceryl stearate, PPG-10 methyl glucose ether, PPG-20 methyl glucose ether, polyoxyethylene-20 sorbitan monoesters, polyoxyethylene-80 castor oil, polyoxyethylene-15 tridecyl ether, polyoxy-ethylene-6 tri-decyl ether, laureth-2, laureth-3, laureth-4, PEG-3 castor oil, PEG 600 dioleate, PEG 400 dioleate, and mixtures thereof.

- 35 -

Numerous other nonionic surfactants are disclosed in McCutcheon's Detergents and Emulsifiers, 1993 Annuals, published by McCutcheon Division, MC Publishing Co., Glen Rock, NJ, pp. 1-246 and 266-272; in the *CTFA International Cosmetic Ingredient Dictionary, Fourth Ed.*, Cosmetic, Toiletry and Fragrance Association, Washington, D.C. (1991) (hereinafter the CTFA Dictionary) at pages 1-651; and in the *CTFA Handbook*, at pages 86-94, each incorporated herein by reference.

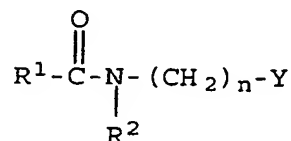
In addition to anionic and nonionic surfactants, cationic, ampholytic, and amphoteric surfactants can be used in the antimicrobial compositions. Cationic surfactants include amine oxides, for example.

Ampholytic surfactants can be broadly described as derivatives of secondary and tertiary amines having aliphatic radicals that are straight chain or branched, and wherein one of the aliphatic substituents contains from about 8 to 18 carbon atoms and at least one of the aliphatic substituents contains an anionic water-solubilizing group, e.g., carboxy, sulfonate, or sulfate. Examples of compounds falling within this description are sodium 3-(dodecylamino)propionate, sodium 3-(dodecylamino)propane-1-sulfonate, sodium 2-(dodecylamino)ethyl sulfate, sodium 2-(dimethylamino)octadecanoate, disodium 3-(N-carboxymethyl-dodecylamino)propane-1-sulfonate, disodium octadecyliminodiacetate, sodium 1-carboxymethyl-2-undecylimidazole, and sodium N,N-bis(2-hydroxyethyl)-2-sulfato-3-dodecoxypropylamine.

- 36 -

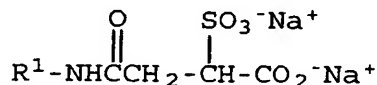
More particularly, one class of ampholytic surfactants include sarcosinates and taurates having the general structural formula

5



10 wherein R^1 is C_{11} through C_{21} alkyl, R^2 is hydrogen or C_1 - C_2 alkyl, Y is CO_2M or SO_3M , M is an alkali metal, and n is a number 1 through 3.

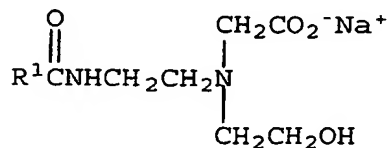
Another class of ampholytic surfactants is the amide sulfosuccinates having the structural
15 formula



20

The following classes of ampholytic surfactants also can be used:

25

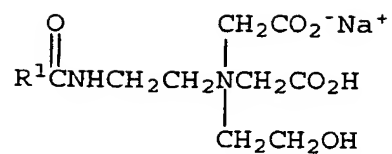


alkoamphoglycinates

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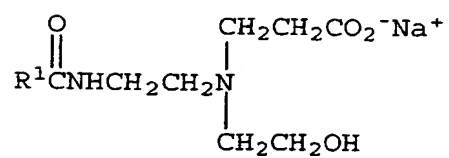
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alkoamphocarboxyglycinates

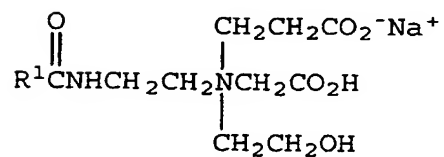
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alkoamphopropionates

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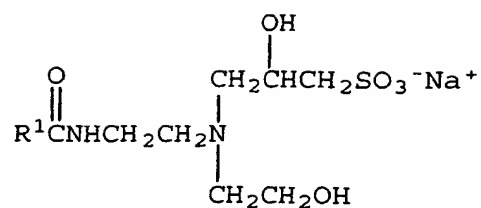


alkoamphocarboxypropionates

25

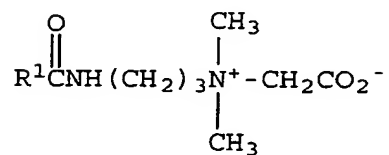
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alkoamphopropylsulfonates

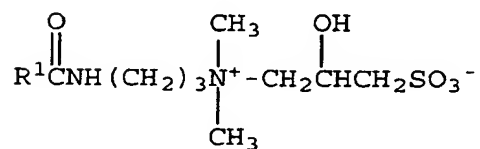
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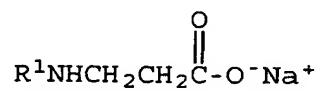
alkamidopropyl betaines

20



alkamidopropyl hydroxysultaine

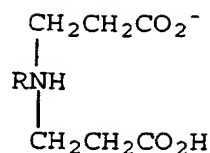
25



30

alkylaminopropionates

- 39 -



5

alkyliminopropionates.

Additional classes of ampholytic surfactants include
 10 the phosphobetaines and the phosphitaines.

Specific, nonlimiting examples of ampholytic surfactants useful in the present invention are sodium coconut N-methyl taurate, sodium oleyl N-methyl taurate, sodium tall oil acid N-methyl
 15 taurate, sodium palmitoyl N-methyl taurate, cocodimethylcarboxymethylbetaine, lauryldimethylcarboxymethylbetaine, lauryldimethylcarboxyethylbetaine, cetyldimethylcarboxymethylbetaine, lauryl-bis-(2-hydroxyethyl)carboxymethylbetaine, oleyldimethyl-
 20 gammacarboxypropylbetaine, lauryl-bis-(2-hydroxypropyl)-carboxyethylbetaine, cocoamidodimethylpropylsultaine, stearylamidodimethylpropylsultaine, laurylamido-bis-(2-hydroxyethyl)propylsultaine, disodium oleamide PEG-2 sulfosuccinate, TEA oleamido
 25 PEG-2 sulfosuccinate, disodium oleamide MEA sulfosuccinate, disodium oleamide MIPA sulfosuccinate, disodium ricinoleamide MEA sulfosuccinate, disodium undecylenamide MEA sulfosuccinate, disodium wheat germamido MEA sulfosuccinate, disodium wheat germ-
 30 amido PEG-2 sulfosuccinate, disodium isostearamideo MEA sulfosuccinate, cocoamphoglycinate, cocoamphocarboxyglycinate, lauroamphoglycinate, lauroamphocarboxyglycinate, capryloamphocarboxyglycinate,

- 40 -

cocoamphopropionate, cocoamphocarboxypropionate,
lauroamphocarboxypropionate, capryloamphocarboxy-
propionate, dihydroxyethyl tallow glycinate,
cocamido disodium 3-hydroxypropyl phosphobetaine,
5 lauric myristic amido disodium 3-hydroxypropyl phos-
phobetaine, lauric myristic amido glyceryl phospho-
betaine, lauric myristic amido carboxy disodium 3-
hydroxypropyl phosphobetaine, cocoamido propyl mono-
sodium phosphitane, lauric myristic amido propyl
10 monosodium phosphitane, and mixtures thereof.

3. Carrier

The carrier in this embodiment comprises
15 water.

4. Optional Ingredients

The optional ingredients discussed in
20 A.4., above, also can be utilized in this embodiment
of the invention, in the same amounts and for the
same purposes.

5. Hydric Solvent and Hydrotrope

25 This embodiment of the present invention
contains 0% to about 25%, by weight, of a hydric
solvent, and 0% to about 30%, by weight, of a
hydrotrope, wherein the antibacterial composition
30 contains at least one of the hydric solvent and
hydrotrope. Preferred embodiments contain both a
hydric solvent and a hydrotrope.

- 41 -

Preferred embodiments contain about 2% to about 20%, by weight, of a hydric solvent and/or about 2% to about 25%, by weight, of a hydrotrope. Most preferred embodiments contain about 5% to about 15%, by weight, of a hydric solvent and/or about 5% to about 20%, by weight, of a hydrotrope.

As defined herein, the term "hydric solvent" is a water-soluble organic compound containing one to six, and typically one to three, hydroxyl groups. The term "hydric solvent" therefore encompasses water-soluble alcohols, diols, triols, and polyols. Specific examples of hydric solvents include, but are not limited to, methanol, ethanol, isopropyl alcohol, n-butanol, n-propyl alcohol, ethylene glycol, propylene glycol, glycerol, diethylene glycol, dipropylene glycol, tripropylene glycol, hexylene glycol, butylene glycol, 1,2,6-hexanetriol, sorbitol, PEG-4, and similar hydroxyl-containing compounds.

A hydrotrope is a compound that has the ability to enhance the water solubility of other compounds. A hydrotrope utilized in the present invention lacks surfactant properties, and typically is a short-chain alkyl aryl sulfonate. Specific examples of hydrotropes includes, but are not limited to, sodium cumene sulfonate, ammonium cumene sulfonate, ammonium xylene sulfonate, potassium toluene sulfonate, sodium toluene sulfonate, sodium xylene sulfonate, toluene sulfonic acid, and xylene sulfonic acid. Other useful hydrotropes include sodium polynaphthalene sulfonate, sodium polystyrene sulfonate, sodium methyl naphthalene sulfonate, and disodium succinate.

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C. **Antibacterial Compositions Containing
an Antibacterial Agent and a Hydric
Solvent and/or a Hydrotrope**

5

In still another embodiment, the antibacterial compositions comprise an active antibacterial agent, and a hydric solvent and/or a hydrotrope. The compositions of embodiment C exhibit a rapid
10 bacteria kill, and also are essentially unlimited in the identity of the surfactant in the composition. The solvent and/or hydrotrope assists in solubilizing the antibacterial agent. Accordingly, at
15 least 25% saturation of the antibacterial agent in the continuous aqueous phase can be achieved even in the absence of a surfactant.

1. **Antibacterial Agent**

20

The amount and identity of the antibacterial agent present in this embodiment of the invention is discussed above in A.1.

25

In addition, similar to embodiment B, in order to achieve the desired bacteria kill in a
short contact time, like 15 to 60 seconds, the continuous aqueous phase of the composition contains an
amount of antibacterial agent that is at least about 25%, and preferably at least about 50%, and more
preferably at least about 75%, of the saturation
30 concentration of the antibacterial agent in water, when measured at room temperature. To achieve the full advantage of the present invention, the continuous aqueous phase is about 95% to 100% saturated with the antibacterial agent.

- 43 -

2. Surfactant

5 The surfactant is an optional ingredient in this embodiment. However, if present, the amount of surfactant present in this embodiment of the present invention is 0% to about 10% by weight, preferably 0% to about 5%, by weight. To achieve the full advantage of the present invention, the surfactant is present in an amount of 0% to about 10 2%, by weight. Due to the presence of a hydric solvent and/or a hydrotrope, the identity of the surfactant in this embodiment is identical to the surfactants disclosed in B.2.

15 3. Carrier

The carrier in this embodiment comprises water.

20 4. Optional Ingredients

The optional ingredients discussed in A.4., above, also can be utilized in this embodiment of the invention, in the same amounts and for the 25 same purposes.

5. Hydric Solvent and Hydrotrope

30 The hydric solvent and hydrotrope discussed in B.5., above, also can be utilized in this embodiment of the invention, for the same purpose. However, the amount of hydric solvent and/or hydrotrope present in this embodiment can be greater than

- 44 -

the amount disclosed in B.5., above, because an additional amount of solvent and/or hydrotrope may be necessary to solubilize the antibacterial agent, in the absence of a surfactant.

5 Therefore, in embodiment C, the compositions can contain 0% to about 60%, by weight, of a hydric solvent, and 0% to about 40%, by weight, of a hydrotrope. However, the composition contains at least one of the hydrotrope and hydric solvent.
10 Preferred embodiments contain about 2% to about 20%, by weight, of a hydric solvent and/or about 2% to about 25%, by weight, of a hydrotrope. Highly preferred embodiments contain about 5% to about 15%, by weight, of a hydric solvent and/or about 5% to about
15 20%, by weight, of a hydrotrope. Most preferred embodiments contain both a hydric solvent and a hydrotrope.

20 **D. Antibacterial Compositions Containing
Antibacterial Agent, a Disinfecting
Alcohol, a Gelling Agent**

25 In another embodiment, the antibacterial compositions comprise an active antibacterial agent, a disinfecting alcohol, and a gelling agent. The compositions of embodiment D exhibit a rapid bacteria kill. The compositions of embodiment D are excellent hand sanitizers.

30

1. **Antibacterial Agent**

The identity of the antibacterial agent in this embodiment of the invention is discussed above

- 45 -

in A.1. In this embodiment, the antibacterial agent is present in an amount of about 0.05% to about 5%, and preferably about 0.1% to about 4%, by weight of the composition. To achieve the full advantage of the present invention, the antibacterial agent is present in an amount of about 0.25% to about 2%, by weight, of the composition.

2. Carrier

10

The carrier in the present composition comprises water.

3. Disinfecting Alcohol

15

Antibacterial compositions of the present invention contain about 1% to about 40%, by weight, of a disinfecting alcohol. Preferred embodiments contain about 2% to about 38%, by weight, of a disinfecting alcohol. Most preferred embodiments contain about 5% to about 30%, by weight, of a disinfecting alcohol.

20

As defined herein, the term "disinfecting alcohol" is a water-soluble alcohol containing one to six carbon atoms. Disinfecting alcohols include, but are not limited to, methanol, ethanol, propanol, and isopropyl alcohol.

25

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4. Gelling Agent

The present antibacterial compositions also contain about 0.01% to about 5%, by weight, and preferably 0.10% to about 3%, by weight, of a gelling agent. To achieve the full advantage of the present invention, the antibacterial compositions contain about 0.25% to about 2.5%, by weight, of a gelling agent. The antibacterial compositions typically contain a sufficient amount of gelling agent such that the composition is a viscous liquid, gel, or semisolid that can be easily applied to, and rubbed on, the skin. Persons skilled in the art are aware of the type and amount of gelling agent to include in the composition to provide the desired composition viscosity or consistency.

The term "gelling agent" as used here and hereafter refers to a compound capable of increasing the viscosity of a water-based composition, or capable of converting a water-based composition to a gel or semisolid. The gelling agent, therefore, can be organic in nature, for example, a natural gum or a synthetic polymer, or can be inorganic in nature.

As previously stated, the present compositions are free of a surfactant. A surfactant is not intentionally added to a present antibacterial composition, but may be present in an amount of 0% to about 0.5%, by weight, because a surfactant may be present in a commercial form of a gelling agent to help dispense the gelling agent in water. A surfactant also may be present as an additive or by-product in other composition ingredients.

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Surfactants are omitted from the present compositions to help avoid micelle formation, which in turn solubilize the active antibacterial compound and reduce its effectiveness. Similarly, preferred gelling agents are those that do not form micelles in particular, and do not complex or bind with the active antibacterial agents, or otherwise adversely effect the antibacterial properties of the antibacterial agent. Regardless of the identity of the gelling agent, the amount of gelling agents and other composition ingredients is selected such that the antibacterial agent is present in an amount of at least 25% of saturation, when measured at room temperature.

The following are nonlimiting examples of gelling agents that can be used in the present invention. In particular, the following compounds, both organic and inorganic, act primarily by thickening or gelling the aqueous portion of the composition:

acacia, acrylates/steareth-20 methacrylate copolymer, agar, algin, alginic acid, ammonium acrylate copolymers, ammonium alginate, ammonium chloride, ammonium sulfate, amylopectin, attapul-gite, bentonite, C9-15 alcohols, calcium acetate, calcium alginate, calcium carrageenan, calcium chloride, caprylic alcohol, carbomer 910, carbomer 934, carbomer 934P, carbomer 940, carbomer 941, carboxymethyl hydroxyethylcellulose, carboxymethyl hydroxypropyl guar, carrageenan, cellulose, cellulose gum, cetearyl alcohol, cetyl alcohol, corn starch, damar, dextrin, dibenzylidene sorbitol, ethylene dihydrogenated tallowamide, ethylene dioleamide, ethylene

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distearamide, gelatin, guar gum, guar hydroxypropyl-trimonium chloride, hectorite, hyaluronic acid, hydrated silica, hydroxybutyl methylcellulose, hydroxyethylcellulose, hydroxyethyl ethylcellulose, hydroxyethyl stearamide-MIPA, hydroxypropylcellulose, hydroxypropyl guar, hydroxypropyl methylcellulose, isocetyl alcohol, isostearyl alcohol, karaya gum, kelp, lauryl alcohol, locust bean gum, magnesium aluminum silicate, magnesium silicate, magnesium trisilicate, methoxy PEG-22/dodecyl glycol copolymer, methylcellulose, microcrystalline cellulose, montmorillonite, myristyl alcohol, oat flour, oleyl alcohol, palm kernel alcohol, pectin, PEG-2M, PEG-5M, polyacrylic acid, polyvinyl alcohol, potassium alginate, potassium aluminum polyacrylate, potassium carrageenan, potassium chloride, potassium sulfate, potato starch, propylene glycol alginate, sodium acrylate/vinyl alcohol copolymer, sodium carboxymethyl dextran, sodium carrageenan, sodium cellulose sulfate, sodium chloride, sodium polymethacrylate, sodium silicoaluminate, sodium sulfate, stearalkonium bentonite, stearalkonium hectorite, stearyl alcohol, tallow alcohol, TEA-hydrochloride, tragacanth gum, tridecyl alcohol, tromethamine magnesium aluminum silicate, wheat flour, wheat starch, xanthan gum, and mixtures thereof.

The following additional nonlimiting examples of gelling agents act primarily by thickening the nonaqueous portion of the composition:

abietyl alcohol, acrylinoleic acid, aluminum behenate, aluminum caprylate, aluminum dilinoleate, aluminum distearate, aluminum isostearates/laurates/palmitates or stearates, aluminum isostear-

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ates/myristates, aluminum isostearates/palmitates, aluminum isostearates/stearates, aluminum lanolate, aluminum myristates/palmitates, aluminum stearate, aluminum stearates, aluminum tristearate, beeswax, behenamide, behenyl alcohol, butadiene/acrylonitrile copolymer, C29-70 acid, calcium behenate, calcium stearate, candelilla wax, carnauba, ceresin, cholesterol, cholesteryl hydroxystearate, coconut alcohol, copal, diglyceryl stearate malate, dihydroabietyl alcohol, dimethyl lauramine oleate, dodecanedioic acid/cetearyl alcohol/glycol copolymer, erucamide, ethylcellulose, glyceryl triacetyl hydroxystearate, glyceryl triacetyl ricinoleate, glycol dibehenate, glycol dioctanoate, glycol distearate, hexanediol distearate, hydrogenated C6-14 olefin polymers, hydrogenated castor oil, hydrogenated cottonseed oil, hydrogenated lard, hydrogenated menhaden oil, hydrogenated palm kernel glycerides, hydrogenated palm kernel oil, hydrogenated palm oil, hydrogenated polyisobutene, hydrogenated soybean oil, hydrogenated tallow amide, hydrogenated tallow glyceride, hydrogenated vegetable glyceride, hydrogenated vegetable glycerides, hydrogenated vegetable oil, hydroxypropylcellulose, isobutylene/isoprene copolymer, isocetyl stearyl stearate, Japan wax, jojoba wax, lanolin alcohol, lauramide, methyl dehydroabietate, methyl hydrogenated rosinatate, methyl rosinatate, methylstyrene/vinyltoluene copolymer, microcrystalline wax, montan acid wax, montan wax, myristyleicosanol, myristyloctadecanol, octadecene/-maleic anhydride copolymer, octyldodecyl stearyl stearate, oleamide, oleostearine, ouricury wax, oxidized polyethylene, ozokerite, palm kernel alco-

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hol, paraffin, pentaerythrityl hydrogenated rosin-
ate, pentaerythrityl rosinate, pentaerythrityl
tetraabietate, pentaerythrityl tetrabehenate, penta-
erythrityl tetraoctanoate, pentaerythrityl tetra-
oleate, pentaerythrityl tetrastearate, phthalic
5 anhydride/glycerin/glycidyl decanoate copolymer,
phthalic/trimellitic/glycols copolymer, polybutene,
polybutylene terephthalate, polydipentene, polyeth-
ylene, polyisobutene, polyisoprene, polyvinyl
10 butyral, polyvinyl laurate, propylene glycol dicap-
rylate, propylene glycol dicocoate, propylene glycol
diisononanoate, propylene glycol dilaurate, propyl-
ene glycol dipelargonate, propylene glycol distear-
ate, propylene glycol diundecanoate, PVP/eicosene
15 copolymer, PVP/hexadecene copolymer, rice bran wax,
stearalkonium bentonite, stearalkonium hectorite,
stearamide, stearamide DEA-distearate, stearamide
DIBA-stearate, stearamide MEA-stearate, stearone,
stearyl alcohol, stearyl erucamide, stearyl stear-
20 ate, stearyl stearoyl stearate, synthetic beeswax,
synthetic wax, trihydroxystearin, triisononanoic,
triisostearin, triisononanoic, triisostearin, tri-
isostearyl trilinoleate, trilaurin, trilinoleic
acid, trilinolein, trimyristin, triolein, tripalmitin,
25 tristearin, zinc laurate, zinc myristate, zinc
neodecanoate, zinc rosinate, zinc stearate, and
mixtures thereof.

5. Optional Ingredients

a. Polyhydric Solvent

A polyhydric solvent, if present at all,
is present in an amount of about 0.1% to about 50%,

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and preferably about 5% to about 50%, by weight of the composition. To achieve the full advantage of the present invention, the polyhydric solvent is present in an amount of about 10% to about 50% by weight of the composition. In contrast to a disinfecting alcohol, a polyhydric solvent contributes little, if at all, to the antibacterial efficacy of the present composition.

As defined herein, the term "polyhydric solvent" is a water-soluble organic compound containing two to six, and typically two or three, hydroxyl groups. The term "water-soluble" means that the polyhydric solvent has a water solubility of at least 0.1 g of polyhydric solvent per 100 g of water at 25°C. There is no upper limit to the water solubility of the polyhydric solvent, e.g., the polyhydric solvent and water can be soluble in all proportions.

The term "polyhydric solvent" therefore encompasses water-soluble diols, triols, and polyols. Specific examples of hydric solvents include, but are not limited to, ethylene glycol, propylene glycol, glycerol, diethylene glycol, dipropylene glycol, tripropylene glycol, hexylene glycol, butylene glycol, 1,2,6-hexanetriol, sorbitol, PEG-4, and similar polyhydroxy compounds.

b. Hydrotrope

A hydrotrope, if present at all, is present in an amount of about 0.1% to about 30%, and preferably about 0.5% to about 25%, by weight of the composition. To achieve the full advantage of the

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present invention, the hydrotrope is present in an amount of about 1% to about 20%, by weight of the composition. The identity of the hydrotropes is discussed in B.5., above, and is used in this embodiment of the invention for the same purpose.

c. Other Optional Ingredients

Other optional ingredients discussed in A.4., above, also can be utilized in this embodiment of the invention, in the same amounts and for the same purposes.

Additional optional ingredients useful in this embodiment include skin conditioners. Examples of skin conditioners, include emollients, such as, cetyl myristate, glyceryl dioleate, isopropyl myristate, lanolin, methyl laurate, PPG-9 laurate, soy stearyl, octyl palmitate, and PPG-5 lanoate, for example. The skin conditioner also can be a humectant, for example, glucamine and pyridoxine glycol, for example. Occlusive skin conditioners, for example, aluminum lanolate, corn oil, methicone, coconut oil, stearyl stearate, phenyl trimethicone, trimyristin, olive oil, and synthetic wax, also can be used. Combinations of the classes of skin conditioners, in addition to miscellaneous skin conditioners known to persons skilled in the art, alone or in combination can be used. Nonlimiting examples of miscellaneous skin conditioners include aloe, cholesterol, cystine, keratin, lecithin, egg yolk, glycine, PPG-12, retinol, salicylic acid, orotic acid, vegetable oil, and soluble animal collagen. The skin conditioners can be used alone, or in com-

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5 bination with a skin protectant, like petroleum, cocoa butter, calamine, and kaolin, for example. A skin protectant also can be used alone. Additional examples of skin conditioners and protectants can be found in "CTFA Cosmetic Ingredient Handbook," J.M. Nikitakis, ed., The Cosmetic, Toiletry and Fragrance Association, Inc., Washington, D.C. (1988) (hereafter CTFA Handbook), pages 79-85, incorporated herein by reference.

10 Antibacterial compositions of the present invention comprising an active antibacterial agent, a disinfecting alcohol, and a hydrotrope exhibit a rapid bacteria kill. The alcohol and hydrotrope assist in solubilizing the antibacterial agent.

15 Accordingly, at least 25% saturation of the antibacterial agent in the composition can be achieved even in the absence of a surfactant.

20 The antibacterial compositions of the present invention do not rely upon a low pH or a high pH to provide a rapid reduction in bacterial populations. Antibacterial compositions of the present invention can have a pH of about 4 to about 9, but at the two extremes of this pH range, the

25 compositions can be irritating to the skin or damaging to other surfaces contacted by the composition. Accordingly, antibacterial compositions of the present invention preferably have a pH of about 5 to about 8, and more preferably about 6 to about 8. To

30 achieve the full advantage of the present invention, the antibacterial compositions have a pH of about 6.5 to about 7.5. In addition, the antibacterial compositions of the present invention also do not

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rely upon a high concentration of disinfecting alcohol.

To demonstrate the new and unexpected results provided by the antibacterial compositions of the present invention, the following Examples and Comparative Examples were prepared, and the ability of the compositions to control Gram positive and Gram negative bacteria was determined. The weight percentage listed in each of the following examples represents the actual, or active, weight amount of each ingredient present in the composition. The compositions were prepared by blending the ingredients, as understood by those skilled in the art and as described below.

The following materials were used as ingredients in the examples. The source of each ingredient, and its abbreviation, are summarized below:

- a) Alkyl (linear) diphenyl oxide disulfonate, Pilot Chemical Co., Santa Fe Springs, CA, CALFAX 10L-45 (active=45.4%),
- b) Alkyl polyglucoside (APG), Henkel Corp., Hoboken, NJ, PLANTAREN 2000N UP (active=55.53%),
- c) Alpha-olefin sulfonate (AOS), Stepan Chemical Co., Northfield, IL, BIOTERGE AS-40 (active=38.80%),
- d) Ammonium lauryl sulfate (ALS), Henkel Corp., STANDAPOL A (active level=28.3%),
- e) Ammonium xylene sulfonate (AXS), Stepan Corp., STEPANATE AXS (active=40%),

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- f) Cocamidopropyl betaine (CAPB),
McIntyre Group, Ltd., Chicago, IL, MACKAM 35-HP
(est. 30% active betaine),
- g) Dipropylene glycol (DPG), Dow Chemi-
5 cal Co., Midland, MI,
- h) Disodium laureth sulfosuccinate
(DSLScct), McIntyre Group, Ltd., MACKANATE EL (ac-
tive=33.8%),
- i) Disodium lauryl sulfosuccinate
10 (DSLrylScct), McIntyre Group, Ltd., MACKANATE LO
(active est.=40%),
- j) DMDM Hydantoin (DMDM), MacIntyre
Group, Ltd., MACKSTAT DM (approx. 55% active),
- k) DowFax Hydrotrope Solution (DFX), Dow
15 Chemical Co., DowFax Hydrotrope Solution (Benzene,
1,1'-oxybis-, sec-hexyl derivatives, sulfonated
sodium salt) (active=45.7%),
- l) Glycerin (GLY), Henkel/Emery,
Cincinnati, OH, Emery 916 Glycerine (99.7% CP/USP),
- 20 m) Isopropanol (IPA), Fisher Scientific,
Pittsburgh, PA, 2-Propanol, HPLC Grade A 451-4,
- n) Lauramine oxide (LAO), McIntyre
Group, Ltd., MACKAMINE LO (active=30.55%),
- o) Liquid Perfume (PF),
- 25 p) Lithium lauryl sulfate (LLS), Henkel,
TEXAPON LLS (active=28.8%),
- q) Magnesium lauryl sulfate (MLS),
Stepan Chemical Co., STEPANOL MG (active=28.3%),
- r) Methyl ester sulfonate (MES), Stepan
30 Chemical Co., ALPHA-STEP ML-40 (Sodium methyl-2
sulfo laurate and disodium 2-sulfo lauric acid)
(active=36.47%),

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- s) Monoethanolamine (MEA), Dow Chemical Co.,
- t) Monoethanolamine lauryl sulfate (MEALS), Albright & Wilson, Cumbria, England,
- 5 EMPICOL LQ 33/F (active=33%),
- u) Octylphenol ethoxylate, 9-10 moles EO (TX100), Union Carbide, TRITON-X 100,
- v) PEG-6ME, polyethylene glycol 300 methyl ether, available from Dow Chemical Co., Mid-
- 10 land, MI, as MPEG 350 (active=est. 100%),
- w) Poloxamer 338 (F108), BASF, Wyandotte, MI, PLURONIC F108 (active=est. 100%),
- x) Potassium cocoate (KCO), McIntyre Group, Ltd., MACKADET 40-K (active=38.4%),
- 15 y) Potassium laurate (KL), prepared from lauric acid (Sigma, #L-4250, active=99.8%) and potassium hydroxide,
- z) Potassium oleate (KO), Norman, Fox & Co., Vernon, CA, NORFOX KO (active=approx. 80%),
- 20 aa) Propylene glycol (PG), Dow Chemical Co., USP Grade (active level=99.96%),
- bb) Sodium 2-ethylhexyl sulfate (S2EHS), Henkel, SULFOTEX OA (active=39.68%),
- cc) Sodium C₁₂-C₁₈ sulfate (SC12-18S),
- 25 Henkel, TEXAPON ZHC needles (active=90.95%),
- dd) Sodium cocoamphoacetate (SCA), McIntyre Group, Ltd., MACKAM IC-90 (active=approx. 32%),
- ee) Sodium cumene sulfonate (SCS), Stepan
- 30 Chemical Co., STEPANATE SCS (active=44.6%),
- ff) Sodium decyl sulfate (SDecS), Henkel, SULFOTEX 110 (active=30.80%),

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- gg) Sodium lauroyl sarcosinate (SLSarc),
Hampshire Chemical Co., Lexington, MA, HAMPOSYL L-30
Type 724 (active=29.9%),
- 5 hh) Sodium lauryl ether sulfate, 1 mole
EO (SLES-1), Henkel, STANDAPOL ES-1 (active=25.40%),
- ii) Sodium lauryl ether sulfate, 2 mole
EO (SLES-2), Henkel, STANDAPOL ES-2 (active
level=25.71%),
- 10 jj) Sodium lauryl sulfate/sodium dodecyl
sulfate (SLS/SDS), BDH Biochemical, BDH Ltd., Poole,
England, (active=99.0%),
- kk) Sodium lauryl sulfoacetate (SLSA),
Stepan Chemical Co., LANTHANOL LAL (active=72.65%),
- 15 ll) Sodium octyl sulfate (SOS), Henkel,
STANDAPOL LF (active=32.90%),
- mm) Sodium salt of NEODOX 23-4 (NDX23-4),
Shell Chemical Co., derived from NEODOX 23-4, a
compound having a 194 molecular weight chain, 4
moles of EO and a carboxylate group (active=94.2%),
- 20 nn) Sodium tridecyl sulfate (SC13S),
Rhodia, Parsippany, NJ, RHODAPON TDS (ac-
tive=24.65%),
- oo) Sodium xylene sulfonate (SXS), Stepan
Chemical Co., STEPANATE SXS (active level=40-42%),
- 25 pp) Triclosan (TCS), IRGASAN DP-300, Ciba
Specialty Chemicals Corp., Greensboro, NC (GC assay
on lots used=99.8-99.9% active TCS; mp=56.0-58.0
C.),
- 30 qq) Triethanolamine lauryl sulfate
(TEALS), Henkel, STANDAPOL T (active=40.1%),
- rr) Tripropylene Glycol (TPG), Dow Chemi-
cal Co., Tripropylene Glycol,

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ss) p-Chloro-m-xyleneol (PCMX), NIPACIDE
PX-R, Nipa Inc., Wilmington, Delaware (about 100%
active),

5 tt) Glyceryl polymethacrylate and propyl-
ene glycol (LUBRAGEL DV), International Speciality
Products, Wayne, New Jersey (about 46% active),

uu) CARBOPOL ULTREZ 10 (ULTREZ 10),
crosslinked polyacrylic acid, BF Goodrich Specialty
Chemicals, Cleveland, Ohio (about 98% active),

10 vv) Diisopropylamine, Air Products and
Chemicals, Allentown, Pennsylvania (about 100% ac-
tive),

ww) LAPONITE XLG (lithium magnesium sil-
icate, synthetic smectite clay), Southern Clay Prod-
15 ucts, Gonzales, Texas (about 99% active),

xx) CELQUAT CS230M (Polyquaternium 10),
National Starch and Chemical Company, Bridgewater,
New Jersey (about 92% active),

yy) Polypropylene glycol-9 (PPG-9), Poly-
20 glycol P425, Dow Chemical Company, Midland, Michigan
(about 100% active),

zz) Ethanol (Denatured Ethyl Alcohol
40B), Gold Shield, Hayward, California (about 100%
active),

25 aaa) Water--Unless otherwise indicated,
the water was prepared as follows: deionized (DI)
water was distilled once through a Corning AG-3
water still.

The following methods were used in the
30 preparation and testing of the examples:

a) Determination of Rapid Germicidal
(Time Kill) Activity of Antibacterial Products. The
activity of antibacterial compositions was measured

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by the time kill method, whereby the survival of challenged organisms exposed to an antibacterial test composition is determined as a function of time. In this test, a diluted aliquot of the composition is brought into contact with a known population of test bacteria for a specified time period at a specified temperature. The test composition is neutralized at the end of the time period, which arrests the antibacterial activity of the composition. The percent or, alternatively, log reduction from the original bacteria population is calculated. In general, the time kill method is known to those skilled in the art.

The composition can be tested at any concentration from 0-100%. The choice of which concentration to use is at the discretion of the investigator, and suitable concentrations are readily determined by those skilled in the art. For example, viscous samples usually are tested at 50% dilution, whereas nonviscous samples are not diluted. The test sample is placed in a sterile 250 ml beaker equipped with a magnetic stirring bar and the sample volume is brought to 100 ml, if needed, with sterile deionized water. All testing is performed in triplicate, the results are combined, and the average log reduction is reported.

The choice of contact time period also is at the discretion of the investigator. Any contact time period can be chosen. Typical contact times range from 15 seconds to 5 minutes, with 30 seconds and 1 minute being typical contact times. The contact temperature also can be any temperature, typically room temperature, or about 25 degrees Celsius.

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The bacterial suspension, or test inoculum, is prepared by growing a bacterial culture on any appropriate solid media (e.g., agar). The bacterial population then is washed from the agar with sterile physiological saline and the population of the bacterial suspension is adjusted to about 10^8 colony forming units per ml (cfu/ml).

The table below lists the test bacterial cultures used in the following tests and includes the name of the bacteria, the ATCC (American Type Culture Collection) identification number, and the abbreviation for the name of the organism used hereafter.

Organism Name	ATCC #	Abbreviation
<i>Staphylococcus aureus</i>	6538	<i>S. aureus</i>
<i>Escherichia coli</i>	11229	<i>E. coli</i>
<i>Klebsiella pneumoniae</i>	10031	<i>K. pneum.</i>
<i>Salmonella choleraesuis</i>	10708	<i>S. choler.</i>

S. aureus is a Gram positive bacteria, whereas *E. coli*, *K. pneum.* and *S. choler.* are Gram negative bacteria.

The beaker containing the test composition is placed in a water bath (if constant temperature is desired), or placed on a magnetic stirrer (if ambient laboratory temperature is desired). The sample then is inoculated with 1.0 ml of the test bacteria suspension. The inoculum is stirred with the test composition for the predetermined contact time. When the contact time expires, 1.0 ml of the test composition/bacteria mixture is transferred

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into 9.0 ml of Tryptone-Histidine-Tween Neutralizer Solution (THT). Decimal dilutions to a countable range then are made. The dilutions can differ for different organisms. Plate selected dilutions in triplicate on TSA+ plates (TSA+ is Trypticase Soy Agar with Lecithin and Polysorbate 80). The plates then are incubated for 25±2 hours, and the colonies are counted for the number of survivors and the calculation of percent or log reduction. The control count (numbers control) is determined by conducting the procedure as described above with the exception that THT is used in place of the test composition. The plate counts are converted to cfu/ml for the numbers control and samples, respectively, by standard microbiological methods.

The log reduction is calculated using the formula

$$\text{Log reduction} = \log_{10}(\text{numbers control}) - \log_{10}(\text{test sample survivors}).$$

The following table correlates percent reduction in bacteria population to log reduction:

% Reduction	Log Reduction
90	1
99	2
99.9	3
99.99	4
99.999	5

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b) Preparation of saturated solutions of TCS in water: A four liter flask was equipped with a 3-inch magnetic stir bar and charged with approximately 7.5 grams (g) TCS and 3 liters (L) of water. The flask then was placed in a water bath, stirred, and heated (40-45°C) for at least 8 hours. The flask containing the resulting TCS/water suspension was removed from the water bath, and the warm suspension filtered through a Coors #32-H porcelain Büchner funnel equipped with Whatman #40 (5.5cm) filter paper. The filtering assembly was attached to a two liter vacuum filter flask, and filtration was conducted in batches. The filtrate then was transferred to another four liter flask and allowed to cool. Typically, fine needles of TCS crystals formed after the filtrate was stored at room temperature for a few days.

For some time kill studies, the TCS solution was refiltered at room temperature before use in the study. For other time kill studies, a small amount of crystalline TCS was allowed to remain in the test container to ensure saturation in the event of a temperature change. It was assumed that TCS crystals present in the time kill test vessel would not affect test results because crystalline TCS is unavailable to act on the bacteria (i.e., is not solubilized).

To determine the concentration of TCS in the water solutions, filtered samples (in triplicate) were analyzed by HPLC. The apparatus used to filter the solutions was a Whatman AUTOVIAL®, with 0.45µm PTFE membrane and glass microfiber prefilter, cat. No. AV125UORG. TCS concentrations were calcu-

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lated using a linear regression line fit (Microsoft EXCEL® software) to TCS/IPA standards included on the same HPLC run.

5 c) Preparation of aqueous TCS/surfactant compositions: A French square bottle was charged with a solution containing a variable concentration of a surfactant and 0.3%, by weight, TCS. The mixture was stirred and heated (35-40°C) for several hours until the TCS was solubilized. Variable
10 transformer-controlled heat lamps were used for warming and the temperature of the solution was monitored with a digital thermometer. Stirring then was stopped, TCS seed crystals (about 1 mg) were added to the solution, and the mixture was allowed
15 to stand at about 20°C. In a few days, crystals were observed on the bottom of solution containers in which the maximum solubility of TCS was exceeded.

The approximate concentration of surfactant necessary to almost completely solubilize
20 the 0.3% TCS was determined by use of an experimental design in which the concentration of surfactant was serially reduced by a factor of two over a series of test samples until the approximate saturation point of TCS in the surfactant was observed.
25 Then the difference in concentration (saturated vs. just solubilized) was halved until a close endpoint for TCS saturation could be determined. The saturation point of TCS/surfactant compositions could be effectively estimated with small-scale (15 to 100
30 mL) samples, but about 600-800 g samples were required to obtain reliable final results. The initial ranges, therefore, were established with

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small-scale samples, and the final concentrations were determined using larger-scale samples.

d) Preparation of compositions containing TCS and a solvent or solvent/hydrotrope combination: TCS first was dissolved in the solvent used in the composition. Water then was added to the TCS/solvent composition, followed by the addition of about 1 mg of TCS seed crystals, and the resulting mixture was allowed to stand at about 20°C to crystallize. In compositions containing a solvent, hydrotrope, and surfactant, the TCS was dissolved in the solvent as above, and then the hydrotrope and surfactant were added to the TCS/solvent solution. The resulting mixture then was diluted to the batch total with water. Adjustment of pH also was performed, if required. The mixture was stirred at room temperature for about an hour, seed TCS was added, and the mixture allowed to stand and crystallize as above. The determination of the TCS saturation point described above also was used (i.e., halving surfactant concentrations). Methods similar to the above for determination of maximum additive concentration have been described in the literature. For example, P.H. Elworthy et al., "Solubilization by surface-active agents and its application in chemistry and biological sciences," Chapman and Hall, Ltd., London, pp. 62-65 (1968), describes determination of concentrations near saturation by observing turbidity of the mixture. A similar technique was used by observing the sample at right angles with a high-intensity light from a small flashlight equipped with a beam focusing attachment (i.e., MINI MAGLITE® AA, MAG Instruments, Califor-

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nia, USA). This method also was used with solutions very near to saturation to enhance observation of small amounts of crystals formed on the bottom of containers.

5 Table 2 summarizes the results of time
kill tests performed on TCS/water compositions. Two
series of results, I and II, demonstrate the effect
of % saturation in TCS/water compositions, i.e.,
that within a given test series, reduction in %
10 saturation produces a concomitant reduction in time
kill efficacy.

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Table 2--Time Kill Results for Saturated TCS/Water Compositions											
			LOG REDUCTION								
		TCS	S. aureus		E. coli		K. pneum.		S. chol.		
	Sample	(g/mL) (by HPLC)	1 min/ or t	5 min.	1 min/ or t	5 min	1 min/ or t	5 min	1 min/ or t	5 min	
I	100% sat'd.	9.3×10^{-7}	1.07/15s	>3.91	0.44/15s	>4.06	0.32/15s	>4.00			
	50% sat'd.	3.9×10^{-7}	0.03/15s	1.71	0.13/15s	1.15	0.21/15s	2.76			
	10% sat'd.	6.7×10^{-8}	0.03/15s	0.02	0.06/15s	0.08	0/15s	0.14			
II	100% sat'd.	9.6×10^{-6}	3.93		1.76		2.85		2.15		
	50% sat'd.	4.9×10^{-6}	0.24		0.26		0.35		1.28		

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Comparing the data in Tables 2 and 3 shows that at the very lowest concentration of TCS (i.e., 5 to 10 ppm), the efficacy of time kill is reduced compared to samples containing higher levels of TCS. For example, a sample in Table 2 containing 0.93 ppm TCS has a log reduction of 0.44 after 15 seconds vs. *E. coli*, whereas a sample in Table 3 containing 484 ppm TCS had a log reduction of 4.13 after 15 seconds vs. the same organism. This effect is more apparent at shorter-contact time periods. Another example, in more complex compositions is illustrated in samples in Table 3, i.e., 50 ppm TCS (est.)/10%PG/5%SXS vs. (448 ppm TCS (est.)/20%PG/10%SXS). The sample with the higher TCS concentration showed at least a log improvement in bacterial reduction after 1 minute. The data in Table 3 also show differences in efficacy when different solvents/hydrotropes are used with approximately the same TCS concentrations.

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Table 3--TCS in Solvent and/or Hydrotrope Systems						
TCS (ppm)	Solvent/ Hydrotrope	<i>S. aureus</i>		<i>E. coli</i>		1 min.
		sec.	1 min.	sec.	1 min.	
112 (est)	17%IPA		>4.42			>3.56
0	17%IPA		0.42			-0.24
110 (est)	23.85%PG		>4.39			2.37
342	40.01%PG	4.97 ¹¹ /30 ²¹	>5.17	4.29/30		>4.67
484	41.86%PG	>3.46/15	>3.46	4.13/15		>4.38
510	42.53%PG	>5.17/30	>5.17	4.47/30		>4.67
723	44.20%PG	>3.46/15	>3.46	>4.38/15		>4.38
603	45.05%PG	>4.69/15	>4.69	4.21/15		>4.65
895	47.52%PG	>5.17/30	>5.17	4.42/30		>4.67
1385	50.00%PG	>4.49/15	>4.49	4.45/15		>4.65
0	50.00%PG	0.15/15	0.13	0.25/15		0.26
0	75.00%PG	1.20/15	2.35	0.35/15		1.73
63	5%SXS		>4.43			0.96
0	5%SXS		0.33			-0.15

Table 3--TCS in Solvent and/or Hydrotrope Systems					
TCS (ppm)	Solvent/ Hydrotrope	<i>S. aureus</i>		<i>E. coli</i>	
		sec.	1 min.	sec.	1 min.
57	5%SCS		3.64		0.80
0	5%SCS		-0.05		-0.11
448 (est)	20%PG/10%SXS	>4.14/30	>4.14	>5.25/30	>5.25
0	20%PG/10%SXS	0.05/30	0.05	1.16/30	1.35
50 (est)	10%PG/5%SXS		3.42		3.18
0	10%PG/5%SXS		0.05		0.35
50 (est)	10%PG/5%SCS		0.59		4.96
0	10%PG/5%SCS		-0.03		0.96
502 (est)	14.5%DPG/10%SXS	>3.63/30	>3.63	>4.44/30	>4.44
0	14.5%DPG/10%SXS	0.03.30	0.04	0.26/30	0.17

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Table 3--TCS in Solvent and/or Hydrotrope Systems						
TCS (ppm)	Solvent/ Hydrotrope	K. pneum.		S. chol.		1 min.
		sec.	1 min.	sec.	1 min.	
112 (est)	17%IPA		>4.11			>3.79
0	17%IPA		0.89			1.23
110 (est)	23.85%PG					
342	40.01%PG	4.33/30	5.29	2.52/30		3.51
484	41.86%PG	2.96/15	>3.44	1.14/15		2.31
510	42.53%PG	4.61/30	>5.64	1.56/30		2.27
723	44.20%PG	>3.44/15	>3.44	1.29/15		2.59
603	45.05%PG	2.60/15	4.79	1.79/15		>4.50
895	47.52%PG	5.26/30	>5.64	2.92/30		4.33
1385	50.00%PG	3.26/15	>5.04	2.69/15		>4.59
0	50.00%PG	0.54/15	0.63	0.17/15		0.24
0	75.00%PG	1.98/15	>3.44	1.34/15		3.56
63	5%SXS					
0	5%SXS					

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Table 3--TCS in Solvent and/or Hydrotrope Systems						
TCS (ppm)	Solvent/ Hydrotrope	K. pneum.		S. chol.		1 min.
		sec.	1 min.	sec.	1 min.	
57	5%SCS					
0	5%SCS					
448 (est)	20%PG/10%SXS	>4.32/30	>4.32	3.17/30	>3.68	
0	20%PG/10%SXS	0.22/30	0.37	0.25/30	1.29	
50 (est)	10%PG/5%SXS					
0	10%PG/5%SXS					
50 (est)	10%PG/5%SCS					
0	10%PG/5%SCS					
502 (est)	14.5%DPG/10%SXS	>4.14/30	>4.14	>4.14/30	>4.14	
0	14.5%DPG/10%SXS	0.34/30	0.39	0.36/30	0.47	

1) log reduction; and

2) seconds.

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Many compositions of the present invention contain a surfactant, which potentially can reduce the efficacy of the antibacterial agent. The following examples show the unexpected benefits
5 achieved by compositions of the present invention.

Example 1

10 In this example, a composition of the present invention was compared to three commercially available antibacterial cleansing compositions in a time kill test using a contact time of 5 minutes. A composition of the present invention (Product A) was a saturated solution containing 0.3% triclosan in a
15 1.5% aqueous sodium lauryl sulfate (SLS). The three commercially available antibacterial compositions having unknown triclosan concentrations, were Jergens Antibacterial (JA) Hand Soap, a product of Andrew Jergens Inc.; Clean and Smooth (CS), a prod-
20 uct of Benckiser; and Soft Soap (SSp), a product of Colgate Palmolive.

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Product	Triclosan (%)	% Saturation ³⁾	Log Reduction at 5 minutes (time kill)			
			<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneum.</i>	<i>S. chol.</i>
A	0.3	100	>4.47	>4.41	>4.36	4.67
JA	Unk.	Unk.	2.48	0.20	0.18	--
CS	Unk.	Unk.	2.80	0.00	0.10	--
SSp	Unk.	Unk.	1.62	0.00	0.20	--

1) "--" means not tested;

2) "Unk." means Unknown; and

3) "% saturation" means percent saturation of TCS in the continuous aqueous phase.

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Example 1 demonstrates the surprising improvement in log reduction of bacteria populations provided by an inventive composition compared to currently available commercial antibacterial compositions. Thus, an aqueous composition containing triclosan in SLS, at 100% saturation, offers significantly greater antibacterial efficacy than any of the three commercial products tested, against Gram positive and against Gram negative microorganisms, both of which can present a significant health threat to consumers.

Example 2

This example demonstrates that the antibacterial activity of an inventive composition is attributable to the active antibacterial agent, as opposed to the surfactant. Test compositions A-1 and A-2 were prepared. Composition A-1 is a solution containing 0.3% triclosan, 1.35% ammonium lauryl sulfate, with the balance being water. Composition A-1 is 100% saturated with triclosan. Composition A-2 is a "placebo," i.e., an aqueous 1.35% ammonium lauryl sulfate solution that is free of the active antibacterial agent.

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Product	Triclosan %	% Saturation	Log Reduction at 5 minutes (time kill)			
			<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneum.</i>	<i>S. chol.</i>
A-1	0.30	100	>3.61	3.16	>4.39	3.73
A-2	0	0	>3.61	0.25	0.15	0.04

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The inventive composition A-1 clearly provided an excellent, broad spectrum antibacterial activity, whereas the "placebo" composition A-2 exhibited an extremely limited spectrum of activity. Composition A-2 has especially poor efficacy against Gram negative organisms. Control of Gram negative organisms is of particular concern to consumers because such organisms present a significant health threat. The excellent broad spectrum activity of composition A-1 clearly shows that the antibacterial activity is unambiguously attributed to the presence of the antibacterial agent in the continuous aqueous phase.

15 Example 3

In this example, a solvent, (i.e., propylene glycol (PG)) was used to solubilize triclosan in an aqueous carrier. No hydrotrope or surfactant was present. Composition A-3 contained 0.0872% by weight triclosan, 47.5% aqueous PG, and the balance being water. Composition A-3 was 100% saturated with triclosan and is a composition of the present invention. Test composition A-4 was a "placebo" consisting of 47.5% PG, by weight, and the balance water. This example illustrates an added advantage of including an optional hydric solvent in the composition. In particular, it was observed that the excellent broad spectrum activity illustrated in earlier examples at contact times of 1 and 5 minutes can be achieved in the presence of the hydric solvent at a contact time of 30 seconds. This example further demonstrates that the antibacterial activity

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of a present composition is unambiguously attributable to the presence of the antibacterial agent.

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Product	Triclosan %	% Saturation	Log Reduction at 30 seconds (time kill)			
			<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneum.</i>	<i>S. chol.</i>
A-3	0.0872	100	>5.17	4.42	5.26	2.92
A-4	0.0	0	0.15	0.25	0.54	0.17

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Example 4

5 This example illustrates that composition
of the present invention provide an acceptable sani-
tization efficacy even though the compositions con-
tain a relatively low concentration of disinfecting
alcohol. Examples B-1, B-3, and B-5 contain 0.15%,
by weight, triclosan, at 100% saturation. Examples
10 B-2, B-4, and B-6 are comparative examples contain-
ing 0% triclosan.

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Ingredient	% (by weight)					
	B-1	B-2	B-3	B-4	B-5	B-6
Triclosan	0.15	0.0	0.15	0.0	0.15	0.0
Ethanol	38	38.0	28.0	28.0	--	--
Dipropylene Glycol	--	--	11.18	11.18	40.0	40.0
ULTREZ 10 ¹⁾	0.3	0.3	0.3	0.3	0.3	0.3
Diisopropylamine	0.05	0.05	0.05	0.05	0.05	0.05
Perfume	0.04	0.04	0.04	0.04	0.04	0.04
Water	Balance	Balance	Balance	Balance	Balance	Balance

¹⁾ added "as is"

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The following table summarizes the results of a time kill test at 15 seconds.

Log Reductions at 15 seconds				
Example	<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneum.</i>	<i>S. chol.</i>
B-1	>4.61	>4.78	>4.51	>4.49
B-2	>4.61	>4.78	>4.51	>4.49
B-3	>4.00	>4.44	>4.20	>3.92
B-4	2.50	1.20	>4.20	>3.92
B-5	>4.39	3.29	1.37	1.30
B-6	0.10	0.0	0.35	0.34

These results show that acceptable sanitization efficacy is achieved, even with reduced levels of disinfecting alcohol and other polyhydric solvents. Furthermore, the compositions of the present invention provide a persistent antibacterial benefit because of the nonvolatile nature of the active ingredient, triclosan, whereas presently marketed compositions do not provide a persistent antibacterial activity.

In particular, Examples B-3 through B-6 demonstrate that the rapid antibacterial activity of the present compositions is attributable mainly to the antibacterial agent, e.g., triclosan, as opposed to a disinfecting alcohol. This is in contrast to prior art disclosures. For example, composition B-3 contains only 28% ethanol, yet exhibits excellent broad-spectrum antibacterial activity at 15 seconds. Composition B-5 contains no alcohol, yet exhibits excellent antibacterial activity against *S. aureus* and *E. coli*. Prior art teachings rely on a high

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alcohol concentration (i.e., >40%) to achieve a fast, broad-spectrum antibacterial activity.

Example 5

5

10 This example illustrates the effect of the identity of the surfactant on the antibacterial activity of the composition. The test results summarized below were performed on a wide variety of compositions containing either an anionic surfactant or representative cationic, anionic/nonionic, amphoteric, and nonionic surfactants. The percent saturation of TCS in the compositions of this example is at least about 90%.

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Surfactant Type	Active Conc.	Surfactant and Amount	S. aureus (1 min)	E. coli (1 min)
Anionic	0.3%TCS	1.6% Sodium Lauryl Sulfate (SLS)	++++	++++
Anionic	0.3%TCS	1.35% Ammonium Lauryl Sulfate (ALS)	++++	+++
Anionic	0.3%TCS	1.5% Triethanolamine Lauryl Sulfate (TEALS)	+++	++++
Anionic	0.3%TCS	5% Sodium Octyl Sulfate (SOS)	++++	++++
Anionic	0.3%TCS	9.5% Sodium 2-Ethylhexyl Sul- fate (S2EHS)	++++	++++
Cationic	0.3%TCS	1.5% Lauramine Oxide (LAO)	++++	++++
Anionic	0.3%TCS	2.5% Sodium Decyl Sulfate (SdecS)	++++	+
Anionic	0.3%TCS	2.5% Sodium Tridecyl sulfate (SCL3S)	++++	0
Anionic	0.3%TCS	1.5% Lithium Lauryl Sulfate (LLS)	++++	0
Anionic	0.3%TCS	1.5% Potassium Cocoate (KCO)	++++	+
Anionic	0.3%TCS	2.0% Methyl Ester Sulfonate (MES)	++++	0
Anionic	0.3%TCS	1.25% Sodium Lauroyl Sarcosinate (SLSarc)	++++	0

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Surfactant Type	Active Conc.	Surfactant and Amount	<i>S. aureus</i> (1 min)	<i>E. coli</i> (1 min)
Anionic	0.3%TCS	1% Sodium Lauryl Sulfoacetate (SLSA)	+++	0
Anionic	0.3%TCS	3% C10 (Linear) Sodium Diphenyl Oxide Disulfonate (L10-45)	++++	0
Anionic	0.3%TCS	1.5% Disodium Lauryl Sulfosuccinate (DSLrylscet)	+++	0
Anionic/Nonionic	0.3%TCS	1.25% Sodium Lauryl Ether Sulfate, 1-mole EO (SLES-1)	++++	0
Anionic/Nonionic	0.3%TCS	1% Sodium Lauryl Ether Sulfate, 2-mole EO (SLES-2)	++++	0
Amphoteric	0.3%TCS	1.25% Sodium Cocoamphoacetate (SCA)	0	0
Amphoteric	0.3%TCS	1.75% Cocamidopropyl Betaine (CAPB)	0	0
Anionic	0.3%TCS	1.25% Alpha-Olefin Sulfonate (AOS)	n/a	0
Anionic	0.3%TCS	1.5% Sodium Alkyl Sulfate, C ₁₂₋₁₈ (SC12-18S)	++	0
Anionic	0.3%TCS	1.5% Magnesium Lauryl Sulfate (MLS)	n/a	0
Anionic/Nonionic	0.3%TCS	2.0% Sodium Myreth-4 Carboxylate (NaNDX23-4)	0	0

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Surfactant Type	Active Conc.	Surfactant and Amount	S. aureus (1 min)	E. coli (1 min)
Anionic/Nonionic	0.3%TCS	1.25% Disodium Laureth Sulfosuccinate (DSLSeet)	++	0
Nonionic	0.3%TCS	2.5% Alkyl Polyglucose (APG)	0	0
Nonionic	0.3%TCS	4% Octoxynol-9 (TX100)	0	0

Key: log reduction in time kill test

++++ >3.99
 +++ >2.99
 ++ >1.99
 + >0.99
 0 <0.99

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The results summarized above demonstrate, unexpectedly, that antibacterial agents and anionic surfactants form highly effective antibacterial compositions when the % saturation of antibacterial agent in the composition is high, i.e., at least 50%. In addition, it was observed that, within a homologous series of surfactants, efficacy can vary (i.e., in the sodium alkyl sulfate homologous series, sodium lauryl sulfate and sodium octyl sulfate yielded high efficacy formulas). The efficacy with respect to the cation also is unexpected (i.e., sodium, ammonium, and triethanolammonium lauryl sulfates provided high efficacy formulas, whereas lithium and magnesium lauryl sulfates did not).

Example 6

The following table summarizes the effect of surfactant identity on the antibacterial activity of the composition. This example expands upon the data provided in Example 5. The table includes results of tests performed on a wide variety of compositions containing either anionic surfactants or representative examples containing cationic, anionic/nonionic, amphoteric, and nonionic surfactants.

The results demonstrate that various anionic surfactants form highly effective systems. The surfactants associated with very high activity (i.e., a high log reduction for both Gram positive (*S. aureus*) and Gram negative (*E. coli*) bacteria) include sodium lauryl sulfate, sodium octyl sulfate, sodium 2-ethylhexyl sulfate and lauramine oxide.

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However, it is possible that the high activity of the lauramine oxide containing composition was due primarily to the surfactant.

Series I (Lauryl Sulfates) demonstrates efficacy effects attributed to the cation. The sodium lauryl sulfate had the highest efficacy, wherein ammonium, monoethanolammonium and triethanolammonium exhibited intermediate efficacy. Lithium and magnesium sulfates exhibited low efficacy. Potassium lauryl sulfate was not tested because of its low solubility at room temperature.

Comparing Series I (Lauryl Sulfates) and Series II (Other Alkyl Sulfates) shows that efficacy varies within a homologous series (i.e., sodium n-alkyl sulfates). Sodium lauryl sulfate and sodium octyl sulfate yield high efficacy formulas, as does the branched chain surfactant, sodium 2-ethylhexyl sulfate.

The data in Series III (Alkyl Carboxylates) suggests that TCS/carboxylate compositions are not highly active against Gram negative bacteria, but are of acceptable activity against Gram positive bacteria.

The results for Series IV (EO-Containing Surfactants) confirm observations that ethylene oxide (EO) in surfactants tends to inactivate TCS. The activity of SLES-1 and SLES-2 vs. *S. aureus* is attributed to the anionic ("lauryl sulfate-like" character) of these anionic/nonionic surfactants.

The results for Series V (Miscellaneous Surfactants) shows that these compositions exhibit moderate to low activity, with the exception of lauramine oxide. The portion of high activity of

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LAO is attributed to the surfactant alone because of its quasi-cationic character. The remaining surfactant/TCS compositions in Series V showed varied activity vs. *S. aureus* (Gram positive) and very
5 little activity vs. *E. coli* (Gram negative).

TCS in Simple Surfactant Systems				
Type	Active Conc.	Other Ingredients	S. aureus (30s/1 min.)	E. coli (30s/1 min.)
Series I--Lauryl Sulfates				
Anionic	0.3%TCS	1.6% sodium lauryl sulfate (SLS)	>3.94/>3.94	4.36/4.36
	0%TCS	1.6% sodium lauryl sulfate (SLS)	>3.94/>3.94	1.51/2.96
Anionic	0.3%TCS	1.35% ammonium lauryl sulfate (ALS)	>3.97/>3.97	1.39/3.95
	0%TCS	1.35% ammonium lauryl sulfate (ALS)	>3.97/>3.97	-0.07/-0.02
Anionic	0.3%TCS	1.5% monoethanolamine lauryl sulfate (MEALS)	2.29/4.03	0.58/2.04
Anionic	0.3%TCS	1.5% triethanolamine lauryl sulfate (TEALS)	2.74/3.73	1.3/4.38
Anionic	0.3%TCS	1.5% lithium lauryl sulfate (LLS)	--/4.1	.51/.81
Anionic	0.3%TCS	1.5% magnesium lauryl sulfate (MLS)	--/--	0.45/0.52
Series II--Other Alkyl Sulfates				
Anionic	0.3%TCS	5% sodium octyl sulfate (SOS)	>4.39/>4.39	>4.83/>4.83
	0%TCS	5% sodium octyl sulfate (SOS)	1.76/1.81	>4.47/>4.47
Anionic	0.3%TCS	9.5% sodium 2-ethylhexyl sulfate (S2EHS)	>4.34/>4.84	>4.47/>4.47
	0%TCS	9.5% sodium 2-ethylhexyl sulfate (S2EHS)	>3.39/>3.39	>4.45/4.35
Anionic	0.3%TCS	2.5% sodium decyl sulfate (SdedS)	>4.39/>4.39	0.59/1.23
Anionic	0.3%TCS	2.5% sodium tridecyl sulfate (SC13S)	3.24/>3.39	-0.04/0.31
Anionic	0.3%TCS	1.5% sodium alkyl sulfate, C12-18 (SC12-18S)	2.09/2.85	0.06/0.01

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TCS in Simple Surfactant Systems				
Type	Active Conc.	Other Ingredients	S. aureus (30s/1 min.)	E. coli (30s/1 min.)
Series III--Alkyl Carboxylates				
Anionic	0.3%TCS	1.5% potassium cocoate (KCO)	>4.34/>4.34	0.35/1.73
Anionic	0.3%TCS	1.0% potassium oleate (KO)	0.55/0.83	-0.08/-0.07
Anionic	0.3%TCS	2.5% potassium oleate (KO)	0.26/0.52	-0.23/-0.23
	0%TCS	2.5% potassium oleate (KO)	-0.15/-0.10	-0.30/0.026
Anionic	0.3%TCS	2.0% potassium laurate (KL)	3.08/3.61	0.10/-0.27
Anionic	0.3%TCS	3.0% potassium laurate (KL)	1.06/1.86	0.82/3.02
	0%TCS	3.0% potassium laurate (KL)	0.18/0.21	1.74/>4.40
Series IV--EO-Containing Surfactants				
Anionic/ Nonionic	0.3%TCS	1.25% sodium lauryl ether sulfate, 1-mole EO (SLES-1)	>4.39/>4.39	0.41/0.46
Anionic/ Nonionic	0.3%TCS	1% sodium lauryl ether sulfate, 2-mole EO (SLES-2)	>4.24/>4.25	0/0.12
Anionic/ Nonionic	0.3%TCS	2.0% sodium myreth-4 carboxylate (NaNDX23-4)	-0.49/-0.49	-0.19/-0.19
Nonionic	0.3%TCS	4% octoxynol-9 (TX100)	0.16/0.15	0.43/0.46

TCS in Simple Surfactant Systems				
Type	Active Conc.	Other Ingredients	S. aureus (30s/1 min.)	E. coli (30s/1 min.)
Series V--Miscellaneous Surfactants				
Cationic	0.3%TCS	1.5% lauramine oxide (LAO)	>4.25/>4.25	>4.63/>4.63
	0%TCS	1.5% lauramine oxide (LAO)	3.55/3.86	4.18/4.73
Anionic	0.3%TCS	1.25% sodium lauroyl sarcosinate (SLSarc)	4.04/>4.34	-0.05/0.04
Anionic	0.3%TCS	1.5% disodium lauryl sulfosuccinate (DSLrylScct)	2.95/4.06	0.02/0.16
Anionic/ Nonionic	0.3%TCS	1.25% disodium laureth sulfosuccinate (DSLScct)	1.76/2.68	0.36/0.38
Anionic	0.3%TCS	1% sodium lauryl sulfoacetate (SLSA)	3.19/3.83	-0.09/-0.03
Anionic	0.3%TCS	2.0% methyl ester sulfonate (MES)	>4.64/>4.64	0.11/0.22
Anionic	0.3%TCS	1.25% alpha-olefin sulfonate (AOS)	1.34/--	0.28/0.33
Anionic	0.3% TCS	3% C10 (linear) sodium diphenyl oxide disulfonate (L10-45)	2.77/4.04	0.18/0.23
Amphoteric	0.3%TCS	1.25% sodium cocoamphoacetate (SCA)	-0.15/-0.20	-0.17/-0.15
Amphoteric	0.3%TCS	1.75% cocamidopropyl betaine (CAPB)	-0.09/-0.03	0.21/0.61
Nonionic	0.3%TCS	2.5% alkyl polyglucose (APG)	-0.10/-0.17	0.01/-0.02

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Example 7

This example illustrates the effect of % saturation of TCS in surfactant compositions (i.e., compositions free of a hydric solvent and hydro-trope). The data summarized in the following table illustrate the effect of % saturation of TCS on the efficacy of TCS in TCS/surfactant/water compositions. Two sections of the table (i.e., TCS/ALS compositions vs. *E. coli* and TCS/SOS compositions vs. *S. aureus*) show a substantial decrease in antibacterial activity with decreasing % saturation. Also, 100% saturated samples (0.15%TCS/0.67%ALS) and (0.15%TCS/4.0%SOS) have an antibacterial activity approaching that of 100% saturated samples containing 0.3% TCS. In these two examples, the effects are seen clearly for organisms wherein the surfactant does not show a strong placebo kill effect.

Effect of % TCS Saturation on Antibacterial Efficacy				
TCS%/Sat'n	Surfactant	Log Reduction		
		<i>S. aureus</i> (30s/1 min)	<i>E. coli</i> (30s/1 min)	<i>K. pneum.</i> (30s/1 min)
0.30/100	1.35%ALS	>3.97/>3.97	1.39/3.95	
0.27/90	1.35%ALS	>3.97/>3.97	0.61/2.89	
0.21/70	1.35%ALS	>3.97/>3.97	0.37/1.54	
0.15/50	1.35%ALS	>3.97/>3.97	0.09/1.17	
0.15/100	0.67%ALS	>3.97/>3.97	1.10/3.63	
0/0	1.35%ALS	>3.97/>3.97	-0.07/-0.02	
0.30/100	1.60%SLS	>3.94/>3.94	4.36/4.36	
0.27/90	1.60%SLS	>3.94/>3.94	4.36/>4.46	
0.21/70	1.60%SLS	>3.94/>3.94	4.04/>4.46	
0.15/50	1.60%SLS	>3.94/>3.94	4.13/>4.46	
0.15/100	0.80%SLS	>3.94/>3.94	3.17/>4.46	
0/0	1.60%SLS	>3.94/>3.94	1.51/2.96	
0.30/100	5.75%SOS	3.39/3.04		>4.44/3.98
0.27/90	5.75%SOS	2.59/3.04		>4.44/>4.44
0.21/70	5.75%SOS	1.59/1.82		>4.44/>4.44
0.15/50	5.75%SOS	0.96/1.43		>4.44/>4.44
0.15/100	4.00%SOS	2.90/3.20		>4.44/>4.44

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Effect of % TCS Saturation on Antibacterial Efficacy				
TCS%/Sat'n	Surfactant	Log Reduction		
		<i>S. aureus</i> (30s/1 min)	<i>E. coli</i> (30s/1 min)	<i>K. pneum.</i> (30s/1 min)
0/0	5.75%SOS	0.23/0.30		>4.44/>4.44

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Example 8

5 This example illustrates a composition of
the present invention that can be used as a hand
cleanser. This example further illustrates an em-
bodiment of the invention wherein the antibacterial
agent is present in combination with a surfactant,
hydric solvent, and hydrotrope. Composition A-5
contains, by weight, 0.3% triclosan, 0.5% ammonium
10 lauryl sulfate, 20% propylene glycol, and 10% sodium
xylene sulfonate, with the balance water. Composi-
tion A-6, by weight, contains 0.1% triclosan, 0.125%
ammonium xylene sulfonate, 20% propylene glycol, and
10% sodium xylene sulfonate the balance being water.
15 Compositions A-5 and A-6 were 100% saturated with
triclosan. Composition A-7 was a "placebo" contain-
ing, by weight, 0.5% ammonium lauryl sulfate, 20%
propylene glycol, 10% sodium xylene sulfate, and the
balance being water.

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Product	Triclosan %	% Saturation	Log Reduction at 30 seconds (time kill)				
			<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneum.</i>	<i>S. chol.</i>	
A-5	0.3	100	>3.84	>4.41	3.56	3.26	
A-6	0.1	100	>3.84	>4.41	3.82	3.95	
A-7	0.0	0	3.22	3.36	0.74	1.77	

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This example illustrates two important features of the present invention. First, the absolute amount of triclosan, or other antibacterial agent, is less important than the percent saturation of antibacterial agent in the composition. For example, composition A-6 (containing 0.10% triclosan) was at least as effective as composition A-5 (containing 0.3% triclosan). The important feature is that both compositions were 100% saturated with triclosan. Second, Example 5 also clearly showed that the active antibacterial agent is responsible for the excellent broad spectrum antibacterial activity. Compositions A-5 and A-6 of the invention clearly outperformed the "placebo" composition A-7, which did not contain an active antibacterial agent.

Example 9

This example demonstrates that a hydric solvent and hydrotrope can impart activity to an otherwise inactive surfactant and antibacterial agent composition. In the following table, all percentages are by weight, and the balance of all compositions is water. Composition B contains 1.35% ammonium lauryl sulfate (ALS) and 0.3% triclosan (TCS). Composition C contains 1.35% ALS and 0.0% TCS. Composition D contains 0.25% ALS, 14.4% DPG, 10.0% SXS, and 0.3% TCS, and Composition E contains 0.25% ALS, 14.4% DPG, 10.0% SXS with 0.0% TCS. Compound F contains 2.5% alkyl polyglucoside (APG™) with 0.3% TCS. Compound G contains 0.3% APG, 14.4% dipropylene glycol (DPG), 10% sodium xylene sulfonate (SXS), and 0.3% TCS. Compound H contains 0.3%

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APG with 14.4% DPG, 10% SXS, and 0.0% TCS. Composition I contains 1.25% sodium cocoamphoacetate (SCA) and 0.3% TCS. Composition J contains 0.25% SCA, 14.4% DPG, 10.0% SXS, and 0.3% TCS. Composition K
5 contains 0.25% SCA, 14.4% DPG, 10.0% SXS, and 0.0% TCS. Composition L contains 1.75% cocamidopropyl betaine (CAPB) and 0.3% TCS. Composition M contains 0.25% CAPB, 14.4% DPG, 10% SXS, and 0.3% TCS. Composition N contains 0.25% CAPB, 14.4% DPG, 10% SXS,
10 and 0.0% TCS. Composition O contains 4% octoxynol-9 (TRITON X-100™, TX100). Composition P contains 0.75% TX100, 14.4% DPG, 10.0% SXS, and 0.3% TCS. Composition Q contains 1.25% sodium lauryl ether sulfate (1 EO, SLES-1) and 0.3% TCS. Composition R
15 contains 0.25% SLES-1, 14.4% DPG, 10.0% SXS, and 0.3% TCS.

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Composition	Triclosan %	Other Ingredients	% Saturation	Log Reduction (Time Kill)	
				S. aureus (30s/60s)	E. coli (30s/60s)
B	0.3	1.35%ALS	~100	>3.97/>3.97	1.39/3.95
C	0.0	1.35%ALS	0	>3.97/>3.97	-0.07/-0.02
D	0.3	0.25%ALS, 14.4%DPG, 10.0%SXS	~100	>3.80/>3.80	>4.38/>4.38
E	0.0	0.25%ALS, 14.4%DPS, 10.0%SXS	~100	1.31/1.54	>2.49/>4.18
F	0.3	2.5%APG	~100	1.19/1.21	>4.69/>4.69
G	0.3	0.3%APG, 14.4%DPG, 10.0%SXS	~100	>4.69/>4.69	4.50/4.58
H	0.0	0.3%APG, 14.4%DPG, 10.0%SXS	0	1.19/1.21	>4.69/>4.69
I	0.3	1.25%SCA	~100	-0.15/-0.20	-0.17/-0.15
J	0.3	0.25%SCA, 14.4%DPG, 10.0%SXS	~100	>4.39/>4.39	>4.73/>4.73
K	0.0	0.25%SCA, 14.4%DPG, 10.0%SXS	0	0.86/0.88	2.90/4.05

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Composition	Triclosan %	Other Ingredients	% Saturation	Log Reduction (Time Kill)	
				<i>S. aureus</i> (30s/60s)	<i>E. coli</i> (30s/60s)
L	0.3	1.75%CAPB	~100	-0.09/-0.03	0.21/0.61
M	0.3	0.25%CAPB, 14.4%DPG, 10.0%SXS	~100	>4.39/>4.39	>4.73/>4.73
N	0.0	0.25%CAPB, 14.4%DPG, 10.0%SXS	0	0.76/0.85	3.26/4.69
O	0.3	4%TX100	~100	0.16/0.15	0.43/0.46
P	0.3	0.75%TX100, 14.4%DPG, 10.0%SXS	~100	0.53/0.58	3.59/>4.73
Q	0.3	1.25%SLES-1	~100	>4.39/>4.39	0.41/0.46
R	0.3	0.25%SLES-1, 14.4%DPG, 10.0%SXS	~100	>4.34/>4.84	>4.47/>4.47

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The results of the time kill tests summarized in the above table very surprisingly show that the use of a hydric solvent and hydrotrope can impart a high antibacterial activity to surfactant/TCS combinations which alone exhibit only low to moderate efficacy (i.e., compare efficacy of composition F vs. G; I vs. J; L vs. M; and Q vs. R). The hydric solvent and hydrotrope also can render active compositions more active in shorter contact times (i.e., compare composition B vs. D). Especially surprising is the observation that a hydric solvent and hydrotrope can impart antibacterial efficacy against *E. coli* even in a composition containing a nonionic surfactant, i.e., octoxynol-9 (compare compositions O vs. P). This result is unexpected because polyethoxylated surfactants are known to inactivate phenolic antibacterial agents.

Example 10

This example demonstrates the importance of % saturation in compositions containing a hydric solvent and hydrotrope. As observed in surfactant/-TCS compositions, the relative % saturation of the antibacterial agent in the continuous aqueous phase of the composition also greatly influences the antibacterial activity of compositions containing a hydric solvent and hydrotrope. As the results summarized below illustrate, this influence on antibacterial activity is especially apparent with respect to the Gram negative bacterium, *K. pneum.*

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Composition	Triclosan %	Other Ingredients	% Saturation
S	0.3	0.25%ALS, 14.4%DPG, 10.0%SXS	~100
T	0.3	0.50%ALS, 14.4%DPG, 10.0%SXS	<S
U	0.3	1.00%ALS, 14.4%DPG, 10.0%SXS	<S, T
V	0.0	1.00%ALS, 14.4%DPG, 10.0%SXS	0
W	0.3	1.20%ALS, 2.5%DPG, 10.0%SXS	~100
X	0.3	2.5%ALS, 2.5%DPG, 10.0%SXS	<W
Y	0.3	5.0%ALS, 2.5%DPG, 10.0%SXS	<W, X
Z	0.0	5.0%ALS, 2.5%DPG, 10.0%SXS	0

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Composition	Log Reduction (time kill)			
	<i>S. aureus</i> (30s/60s)	<i>E. coli</i> (30s/60s)	<i>K. pneum.</i> (30s/60s)	<i>S. chol.</i> (30s/60s)
S	>3.62/>3.62	>4.59/>4.59	2.64/>3.84	>3.85/>3.85
T	>3.62/>3.62	>4.59/>4.59	2.43/3.69	>3.85/>3.85
U	1.67/2.31	>4.59/>4.59	0.89/1.93	3.50/>3.85
V	1.10/1.29	3.42/4.59	0.28/0.67	2.17/>3.85
W	--	--	--	4.19/4.39
X	--	--	--	2.83/3.99
Y	--	--	--	2.39/3.22
Z	--	--	--	1.80/2.52

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From the above data, it is clear that an increase in antibacterial efficacy, as measured by a time kill test, is associated with an increasing % saturation of the antibacterial agent in the aqueous phase of a given composition. This example further shows that compositions containing an antibacterial agent, surfactant, hydric solvent, and hydrotrope are effective when a high % saturation of active antibacterial agent is maintained.

Example 11

This example, in conjunction with Example 10, illustrates the effect of % saturation of TCS in compositions containing a hydric solvent, hydro-trope, and surfactant. As previously observed with simple surfactant/TCS compositions, the relative % saturation of the antibacterial agent in the composition also influences the antibacterial activity of a composition containing a hydric solvent and/or a hydrotrope. From the data summarized in the table of Example 10 and the following table, it is clear that a substantial gain in antibacterial efficacy (as measured by a time kill test) is associated with an increasing % saturation of the antibacterial agent in a given type of composition. The tables demonstrate this effect from two different perspectives. The table in Example 10 shows the effect of changing the concentration of surfactant while maintaining the amount of other composition components constant. The following table shows the effect of varying the concentration of TCS while the concentration of all other components is kept constant.

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In the table of Example 10, the information relating to % saturation is relative because % saturation is difficult to directly calculate. Even using this qualitative data, the effect of % saturation of TCS
5 is clear from both tables for all organisms tested.

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Activity Dependence on % Saturation of TCS in Hydric Solvent/Hydrotrope/Surfactant Compositions				
Triclosan %	Other Ingredients	% Saturation	Log Reduction (Time Kill)	
			<i>S. aureus</i> (30s/60s)	<i>K. pneum.</i> (30s/60s)
0.413	5%DPG, 15%SXS, 0.75%ALS	100	>4.55/>4.55	>3.81/>3.81
0.372	5%DPG, 15%SXS, 0.75%ALS	90	>4.55/>4.55	3.81/>3.81
0.330	5%DPG, 15%SXS, 0.75%ALS	80	>4.55/>4.55	3.46/>3.81
0.300	5%DPG, 15%SXS, 0.75%ALS	73	>4.55/>4.55	3.40/>3.81
0.248	5%DPG, 15%SXS, 0.75%ALS	60	3.02/4.05	2.73/>3.81
0.207	5%DPG, 15%SXS, 0.75%ALS	50	1.96/3.05	2.45/>3.81
0.166	5%DPG, 15%SXS, 0.75%ALS	40	1.94/2.15	2.30/>3.81
0.103	5%DPG, 15%SXS, 0.75%ALS	25	1.72/1.93	1.34/2.78

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Example 12

5 This example illustrates the effect of
different levels of hydric solvent and hydrotrope on
antibacterial efficacy. In particular, the data
summarized below demonstrates the effect of varying
the relative amounts of hydric solvent and hydro-
trope. It should further be noted that the addition
of a perfume (PF) and/or a preservative (DMDM) to
10 the composition has only a modest effect, if any, on
the antibacterial efficacy of the compositions.

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Composition	Triclosan %	Other Ingredients	Log Reduction (Time Kill)			
			S. aureus (30s/60s)	E. coli (30s/60s)	K. pneum. (30s/60s)	S. cholera. (30s/60s)
CCC	Calc 0.0502	14.5%DPG, 10.0%SXS	>3.63/>3.63	>4.44/>4.44	>4.14/>4.14	>4.14/>4.14
DDD	0.0	14.5%DPG, 10.0%SXS	0.03/0.04	0.26/0.17	0.34/0.39	0.36/0.47
E	0.0	0.25%ALS, 14.4%DPG, 10.0%SXS	1.31/1.54	2.49/4.18	0.41/0.78	2.62/>4.04
S	0.3	0.25%ALS, 14.4%DPG, 10.0%SXS	>3.62/>3.62	>4.59/>4.59	2.64/>3.84	>3.85/>3.85
T	0.3	0.50%ALS, 14.4%DPG, 10.0%SXS	>3.62/>3.62	>4.59/>4.59	2.43/3.69	>3.85/>3.85
U	0.3	1.00%ALS, 14.4%DPG, 10.0%SXS	1.67/2.31	>4.59/>4.59	0.89/1.93	3.50/>3.85
V	0.0	1.00%ALS, 14.4%DPG, 10.0%SXS	1.10/1.29	3.42/4.59	0.28/0.67	2.17/>3.85
AA	0.3	0.75%ALS, 5.0%DPG, 10.0%SXS			0.95/2.00	
BB	0.3	0.75%ALS, 5.0%DPG, 12.5%SXS			1.77/3.36	
CC	0.3	0.75%ALS, 5.0%DPG, 15.0%SXS			3.49/>3.69	
DD	0.3	0.75%ALS, 5.0%DPG, 17.5%SXS			>3.69/>3.69	
EE	0.3	0.75%ALS; 5.0%DPG, 20.0%SXS			>3.69/>3.69	
FF	0.3	0.75%ALS, 7.5%DPG, 10.0%SXS			0.81/2.87	
GG	0.3	0.75%ALS, 7.5%DPG, 12.5%SXS			1.72/4.21	
HH	0.3	0.75%ALS, 7.5%DPG, 15.0%SXS			3.04/4.31	
II	0.3	0.75T%ALS, 7.5%DPG, 17.5%SXS			>4.41/>4.41	

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Composition	Triclosan %	Other Ingredients	Log Reduction (Time Kill)			
			S. aureus (30s/60s)	E. coli (30s/60s)	K. pneum. (30s/60s)	S. choler. (30s/60s)
JJ	0.3	0.75%ALS, 7.5%DPG, 20.0%SXS			>4.41/>4.41	
KK	0.3	1.0%ALS, 5.0%DPG, 10.0%SXS			0.08/1.49	
LL	0.3	1.0%ALS, 5.0%DPG, 12.5%SXS			0.97/3.32	
MM	0.3	1.0%ALS, 5.0%DPG, 15.0%SXS			2.57/>4.41	
NN	0.3	1.0%ALS, 5.0%DPG, 17.5%SXS			>4.41/>4.41	
OO	0.3	1.0%ALS, 5.0%DPG, 20.0%SXS			>4.41/>4.41	
PP	0.3	1.0%ALS, 7.5%DPG, 10.0%SXS			0.17/0.92	
QQ	0.3	1.0%ALS, 7.5%DPG, 12.5%SXS			0.92/2.94	
RR	0.3	1.0%ALS, 7.5%DPG, 15.0%SXS			2.92/>3.69	
SS	0.3	1.0%ALS, 7.5%DPG, 17.5%SXS			>3.69/>3.69	
TT	0.3	1.0%ALS, 7.5%DPG, 20.0%SXS			>3.69/>3.69	
UU	0.3	0.75%ALS, 5.0%DPG, 15.0%SXS	3.79/>4.64	>4.57/>4.57	4.07/>4.69	>3.97/>3.97
VV	0.3	0.75%ALS, 5.0%DPG, 15.0%SXS	3.07/3.76	4.01/>4.34	3.40/>4.46	>4.04/>4.04
WW	0.0	0.75%ALS, 5.0%DPG, 15.0%SXS	0.79/0.90	>4.34/>4.34	0.41/1.53	>4.04/>4.04
XX	0.3	0.75%ALS, 10.0%DPG, 10.0%SXS		>4.78/>4.78	0.67/1.46	
YY	0.3	0.75%ALS, 10.0%DPG, 20.0%SXS		>4.78/>4.78	>4.17/>4.17	
ZZ	0.0	0.75%ALS, 10.0%DPG, 20.0%SXS		>4.78/>4.78	>4.17/>4.17	

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Composition	Triclosan %	Other Ingredients	Log Reduction (Time Kill)			
			<i>S. aureus</i> (30s/60s)	<i>E. coli</i> (30s/60s)	<i>K. pneum.</i> (30s/60s)	<i>S. choler.</i> (30s/60s)
AAA	0.3	0.75%ALS, 14.4%DPG, 10%SXS		>4.95/>4.95		
BBB	0.0	0.75%ALS, 14.4%DPG		0.28/0.28		

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It was observed that for compositions S, T, and U, the antibacterial activity against *S. aureus* and *K. pneum.* increases, especially, with a decreasing wt% of ALS surfactant (i.e., an increase in % saturation of TCS). Compositions CC, HH, MM, and RR demonstrate that about 15% SXS, or more, is preferred to exhibit high activity against *K. pneum.* in compositions containing a hydric solvent and a hydrotrope. This observation suggests that the hydrotrope may be acting as an adjuvant for the TCS because the time required for a substantial antibacterial kill, i.e., log reduction of at least 2, is reduced.

15 Example 13

The data summarized in the following table support a theory that the two primary factors for improved antibacterial efficacy are the relative amounts of surfactant and hydrotrope to the amount of antibacterial agent in compositions containing a surfactant, hydric solvent, and antibacterial agent. A higher percentage of surfactant can reduce the % saturation, and thereby decrease the antimicrobial activity of the composition. On the other hand, a higher percentage of hydrotrope appears to provide a higher activity against certain organisms, like *K. pneum.* and *S. choler.* It is theorized that the higher percentage of hydrotrope in the composition provides a greater amount of active antibacterial compound in the aqueous (i.e., nonmicellar) phase of the composition, thereby providing a higher time kill activity. The solvent, therefore, may be act-

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ing as both an additive to enhance antimicrobial activity and to provide better physical stability in these compositions.

Composition	Triclosan %	Other Ingredients	Log Reduction (Time Kill)			
			S. aureus (30s/60s)	E. coli (30s/60s)	K. pneum. (30s/60s)	S. choler. (30s/60s)
CCC	Calc. 0.0502	14.5%DPG, 10.0%SXS	>3.63/>3.63	>4.44/>4.44	>4.14/>4.14	>4.14/>4.14
DDD	0.0	14.5%DPG, 10.0%SXS	0.03/0.04	0.26/0.17	0.34/0.39	0.36/0.47
EEE	0.3%TCS	0.25%ALS, 14.4%DPG, 10.0%SXS	>3.80/>3.80	>4.38/>4.38	3.54/>4.07	>4.04/>4.04
FFF	0%TCS	0.25%ALS, 14.4%DPG, 10.0%SXS	1.31/1.54	2.49/4.18	0.41/0.78	2.62/>4.04
GGG	0.3%TCS	0.25%ALS, 14.4%DPG, 10.0%SXS	>3.62/>3.62	>4.59/>4.59	2.64/>3.84	>3.85/>3.85
HHH	0.3%TCS	0.5%ALS, 14.4%DPG, 10.0%SXS	>3.62/>3.62	>4.59/>4.59	2.43/3.69	>3.85/>3.85
III	0.3%TCS	1%ALS, 14.4%DPG, 10.0%SXS	1.67/2.31	>4.59/>4.59	0.89/1.93	3.50/>3.85
JJJ	0%TCS	1%ALS, 14.4%DPG, 10.0%SXS	1.10/1.29	3.42/4.59	0.28/0.67	2.17/>3.85
KKK	0.4%TCS	0.25%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF	>4.59/>4.59	>4.70/>4.70	4.11/>4.41	>4.04/>4.04
LLL	0.3%TCS	0.25%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF	>4.59/>4.59	>4.70/>4.70	4.06/>4.41	>4.04/>4.04
MMM	0%TCS	0.25%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF	1.70/2.19	3.97/>4.70	0.50/1.43	3.04/>4.04

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Composition	Triclosan %	Other Ingredients	Log Reduction (Time Kill)			
			S. aureus (30s/60s)	E. coli (30s/60s)	K. pneum. (30s/60s)	S. choler. (30s/60s)
NNN	0.3%TCS	0.25%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF	>4.77/4.57	>4.71/>4.71	3.90/>4.55	>4.20/>4.20
OOO	0.3%TCS	1%ALS, 14.4%DPG, 10.0%SXS, 0.5%PF	3.18/4.09	>4.71/>4.71	1.11/3.62	3.90/>4.20
PPP	0.3%TCS	0.5%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF	4.39/>4.77	>4.71/>4.71	3.00/>4.55	>4.20/>4.20
QQQ	0%TCS	1%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF	2.42/3.07	3.03/>4.71	0.65/0.98	2.29/4.10
RRR	0.3%TCS	0.5%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF	>4.71/>4.71	>4.61/>4.61	2.10/3.97	>3.87/>3.87
SSS	0.3%TCS	0.6%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF	>4.71/>4.71	4.61/>4.61	1.46/3.62	>3.87/>3.87
TTT	0.3%TCS	0.75%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF	4.28/>4.71	>4.61/>4.61	1.42/3.34	>3.87/>3.87
UUU	0.3%TCS	0.35%ALS, 10.0%DPG, 10.0%SXS, 0.05%PF	>4.23/>4.23	>4.62/>4.62	3.30/4.63	>3.87/>3.87
VVV	0.3%TCS	0.5%ALS, 10.0%DPG, 10.0%SXS, 0.05%PF	>4.23/>4.23	>4.62/>4.62	2.86/4.18	>3.87/>3.87
WWW	0.3%TCS	0.5%ALS, 7.5%DPG, 10.0%SXS, 0.05%PF	>4.23/>4.23	>4.62/>4.62	2.63/3.77	>3.87/>3.87

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Composition	Triclosan %	Other Ingredients	Log Reduction (Time Kill)			
			<i>S. aureus</i> (30s/60s)	<i>E. coli</i> (30s/60s)	<i>K. pneum.</i> (30s/60s)	<i>S. choler.</i> (30s/60s)
XXX	0.3%TCS	0.6%ALS, 7.5%DPG, 10.0%SXS, 0.05%PF	>4.23/>4.23	>4.62/>4.62	2.45/3.15	>3.87/>3.87
YYY	0.3%TCS	0.5%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF, 0.25%DMDM	>3.83/>3.83	>4.41/>4.41	2.89/>3.76	>3.59/>3.59
ZZZ	0%TCS	0.5%ALS, 14.4%DPG, 10.0%SXS, 0.05%PF, 0.25%DMDM	1.48/2.10	3.84/>4.41	0.38/1.12	2.09/3.45
AAAA	0.3%TCS	0.75%ALS, 5.0%DPG, 10.0%SXS, 0.05%PF	>4.07/>4.07	3.90/4.03	1.97/3.66	3.24/3.24
BBBB	0.3%TCS	0.75%ALS, 5.0%DPG, 7.5%SXS, 0.05%PF	>4.07/>4.07	3.10/4.28	0.25/2.23	0.91/2.80
CCCC	0.3%TCS	0.75%ALS, 7.5%DPG, 10.0%SXS, 0.05%PF	>4.07/>4.07	3.82/>4.53	1.49/3.56	2.93/>3.34
DDDD	0.3%TCS	0.75%ALS, 7.5%DPG, 7.5%SXS, 0.05%PF	>4.07/>4.07	3.47/4.18	0.19/2.00	0.99/2.76

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Example 14

5 This example shows that other hydric sol-
vents can be used in a composition of the present
invention.

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Composition	Triclosan %	Other Ingredients	Log Reduction (Time Kill)			
			S. aureus (30s/60s)	E. coli (30s/60s)	K. pneum. (30s/60s)	S. choler. (30s/60s)
EEEE	0.3	0.75%ALS, 5.0% tripropylene glycol (TPG), 10.0%SXS	4.24/3.91	>4.73/>4.73	--	--
FFFF	0.3	0.75%ALS, 10.0%TPG, 10.0%SXS	2.59/3.65	>4.73/>4.73	--	--
GGGG	0.0	0.75%ALS, 10.0%TPG, 10.0%SXS	0.77/1.11	3.60/4.40	--	--
HHHH	0.3	0.75%ALS, 14.4% propylene glycol (PG), 10.0%SXS	>4.44/>4.44	4.58/>4.78	--	--
IIII	0.3	1.0%ALS, 10.0%PG, 10.0%SXS	>4.44/>4.44	4.48/>4.78	--	--
JJJJ	0.3	0.5%ALS, 20.0%PG, 10.0%SXS	>3.99/>3.99	>4.45/>4.55	3.66/>4.04	3.23/>3.68
KKKK	0.1	0.5%ALS, 20.0%PG, 10.0%SXS	>3.99/>3.99	3.75/>4.55	1.08/3.13	1.51/2.84
LLLL	0.0	0.5%ALS, 20.0%PG, 10.0%SXS	>3.99/>3.99	2.58/4.14	0.25/.072	1.28/2.36
MMMM	0.1	0.12%ALS, 20.0%PG, 10.0%SXS	>3.84/>3.84	>4.41/>4.41	3.82/>3.92	3.95/>3.95
NNNN	0.3	0.5%ALS, 20.0%PG, 10.0%SXS	>3.84/>3.84	>4.41/>4.41	3.56/>3.92	3.26/>3.95
OOOO	0.0	0.5%ALS, 20.0%PG, 10.0%SXS	3.22/3.84	3.36/>4.41	0.74/1.49	1.77/2.93
PPPP	0.3	0.8%SLS, 10.0%PG, 5.0%SXS	>4.11/>4.11	2.50/>3.61	--	--
QQQQ	0.0	0.8%SLS, 10.0%PG, 5.0%SXS	2.67/3.91	1.19/2.40	--	--
RRRR	0.3	0.8%ALS, 10.0%PG, 5.0%SXS	>4.11/>4.11	1.66/3.25	--	--

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Composition	Triclosan %	Other Ingredients	Log Reduction (Time Kill)			
			S. aureus (30s/60s)	E. coli (30s/60s)	K. pneum. (30s/60s)	S. choler. (30s/60s)
SSSS	0.0	0.8%ALS, 10.0%PG, 5.0%SXS	2.28/3.03	0.79/1.63	--	--
TTTT	0.26	0.9%ALS, 10.0%PG, 5.0%SXS	>4.24/>4.25	0.16/0.93	-0.02/0.07	0.53/0.33
UUUU	0.0	0.9%ALS, 10.0%PG, 5.0%SXS	2.53/>4.25	0.06/0.21	0.10/0.00	0.17/0.13

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In addition to the observation that other solvents (e.g., PG and TPG) can be used in compositions of the present invention, products JJJJ through OOOO illustrate another effect of relative saturation of antibacterial agent in the system. The relative % saturation (highest to lowest) of the first three compositions is JJJJ>KKKK>LLLL. Composition KKKK has one-third the amount of TCS as composition JJJJ solubilized in the same level of ALS (0.5%), and compositions LLLL contains 0% TCS. Significant reductions in activity were observed with respect to *K. pneum.* and *S. choler.* when the relative % saturation of TCS in the composition decreases. It also was observed that when the relative % saturation is essentially equal (i.e., about 100%), the activity remains essentially constant even though the absolute amount of TCS in the composition is decreased (i.e., compare Compositions MMMM to NNNN). These data further support the observations with respect to the importance of % saturation set forth in Example 7.

In addition, a comparison of composition IIII to composition TTTT shows that composition TTTT contains slightly less ALS (0.9% vs. 1.0% for IIII), the same amount of PG (10.0%), and one-half the amount of SXS (5.0% vs. 10.0% for IIII). Experimental observations indicated that compositions IIII and TTTT were at or near 100% saturation. However, the log reductions of *E. coli* were considerably lower (about 4 log) for Composition TTTT. This observation further supports the data set forth in Example 8 wherein minimum level of hydrotrope may be

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needed for a high antibacterial efficacy against at least some Gram negative bacteria.

Example 15

5

The following compositions 15-A through 15-D were prepared to demonstrate the superior germ kill provided by compositions of the present invention compared to control compositions (i.e., compositions free of an antibacterial agent), even when very low amounts of disinfecting alcohol are present. Compositions 15A-15D were prepared using standard mixing techniques known in the art. Table 4 below lists the composition ingredients. Table 5 below summarizes the antibacterial efficacy of compositions 15-A through 15-D, as measured in a time kill test.

20

25

Table 4					
Composition	% by weight (as active substance)				
	TCS	Ethanol	PPG-9	DPG	Water
15-A (control)	0	25.86	11.5	--	Balance
15-B	0.10	25.86	11.5	--	Balance
15-C (control)	0	23.0	--	11.18	Balance
15-D	0.10	23.0	--	11.18	Balance

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Table 5				
Composition	Log reduction @ 15 sec/30 sec			
	<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneum.</i>	<i>S. chol.</i>
15-A	0.55/1.73	0.18/0.43	1.15/0.71	2.51/4.24
15-B	3.27/>4.43	3.75/>4.51	1.33/3.10	4.09/4.34
15-C	0.01/0.0	0.17/0.12	0.4/0.11	0.18/0.17
15-D	>4.43/>4.43	3.20/3.48	3.19/4.03	2.86/3.99

Example 15 illustrates the surprisingly high efficacy of compositions of the present invention (15-B and 15-D), wherein high log reductions are observed against both Gram positive and Gram negative bacteria, even for compositions containing less than 26% ethanol. The results are in contrast to compositions described in prior disclosures, wherein high alcohol concentrations (i.e., greater than about 40%) are relied upon to achieve a high, broad spectrum antibacterial activity.

Example 16

Example 16 shows that compositions of the present invention provide excellent, broad spectrum antibacterial activity, even at further reduced alcohol concentrations. Accordingly, composition 16-A containing 0.15% TCS, 11.18% ethanol, 25.71% DPG, the balance being water (as weight percent of active compounds), was prepared. For comparison, an identical control composition 16-B was prepared, except composition 16-B was free of TCS. The following table summarizes the results of antibacterial

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efficacy of compositions 16-A and 16-B by time kill tests.

Composition	Log reduction @ 15 sec/30 sec			
	<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneum.</i>	<i>S. chol.</i>
16-A	4.54/>4.69	>4.78/>4.78	3.63/>4.11	1.12/1.31
16-B	0.88/0.97	0.36/0.37	0.0/0.0	0.0/0.0

Example 16 further demonstrates that the concentration of alcohol in the present compositions can be reduced to very low levels without sacrificing antibacterial activity. Accordingly, compositions that provide excellent antibacterial efficacy, and that do not dry the skin, can be prepared. Prior compositions that relied on a high alcohol concentration for antibacterial activity dried the skin, and often caused skin irritation.

Example 17

Example 17 demonstrates that highly effective compositions of the present invention can incorporate p-chloro-m-xlenol (PCMX) as the antibacterial active agent. Composition 17-A was prepared by admixing 0.1% PCMX, 13.42% ethanol, and the balance water (as weight percent of active compounds). The antibacterial efficacy of composition 17-A was evaluated by a time kill test and exhibited log reductions against *S. aureus*, *E. coli*, *K. pneum.*, and *S. chol.*, at 30 seconds contact time, of 4.16, >4.34, 3.99, and >4.04, respectively. Thus, composition 17-A is a highly effective antibacterial

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composition, even though the composition contained a very low concentration of ethanol.

Example 18

5

Example 18 illustrates a composition of the present invention containing a cationic gelling agent, CELQUAT CS-230M. Composition 18-A was prepared by admixing 0.15% TCS, 28% ethanol, 11.18% DPG, and 2% CELQUAT CS-230M, and the balance was water (as weight percent of active compounds, except CELQUAT, which is "as-is"). The antibacterial efficacy of composition 18-A was evaluated by a time kill test. Composition 18-A demonstrated the following log reductions against *S. aureus*, *E. coli*, *K. pneum.*, and *S. chol.*, at 30 seconds contact time of >3.83, 4.33, >4.43, and >3.55, respectively. Thus, composition 18-A is a highly effective antibacterial composition, even though the composition contained a very low concentration of ethanol.

20

Example 19

Compositions of the present invention can contain a wide variety of gelling agents, hydric solvents, and antibacterial active agents, illustrated by the following examples. In Table 6 below, all weight percentages are as active material, except where indicated by a "*", which indicates an "as-is" weight. The compositions were prepared by mixing and gel preparation techniques well known to persons skilled in the art. The compositions exhibited acceptable clarity, stability, and performance.

30

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Table 6										
Composition	A	B	C	D	E	F	G	H	I	J
Ingredient										
TCS	0.1	0.1	0.1	0.1	0.1	0.1	0.1	0.15	0.1	0.11
Deionized Water	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs
LUBRAGEL DV*	15	15	10	10	10	10	10	10	10	
IPA	18.5									24.93
Propylene Glycol	14	14	14							
Ethanol		23	23	23		23		34.25	23	
PPG-9				11.5	36					
DPG						11.18	35		11.18	
Perfume									0.5	
LAPONITE XLG*										1.5
CELQUAT CS-230M*										
PCMX										
ULTREZ 10*										
Diisopropylamine										

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Table 6

Composition	K	L	M	N	O	P	Q	R	S	T
Ingredient										
TCS	0.1	0.1	0.1	0.1	0.1	0.1	0.1			
Deionized Water	qs	qs	qs	qs	qs	qs	qs	qs	qs	qs
LUBRAGEL DV*										
IPA		18.5	18.5							
Propylene Glycol	44.2	14	14							
Ethanol				23	35	28	28	23	28.07	4.1
PPG-9								14.14	11.16	7.26
DPG				11.18		11.18	11.18			
Perfume					0.04	0.2	0.04			
LAPONITE XLG*	1.5	1.5	2							
CELQUAT CS-230M*				2.5	2	2	2			
PCMX								0.1	0.15	0.1
ULTREZ 10*								0.3	0.3	0.3
Diisopropylamine								0.05	0.05	0.05

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The data presented in all the above tables and examples show that % saturation of antibacterial agent in the aqueous phase of the composition can be directly correlated to a log reduction of bacteria.

5 For example, as shown in the prior tables, a composition having 50% saturation of TCS in the aqueous phase demonstrates a log reduction versus *S. aureus* of 1.96 (30 seconds) and 3.05 (60 seconds) and a log reduction versus *E. coli* of 2.45 (30 seconds) and

10 greater than 3.81 (60 seconds). A 75% saturated and a 100% saturated composition exhibited a log reduction of greater than 4.55 (30 and 60 seconds) vs. *S. aureus* (i.e., a log reduction in excess of the detection limit of the assay). The 75% and 100% saturated

15 compositions exhibited a log reduction of 3.40 (30 seconds) and greater than 3.81 (60 seconds) and greater than 3.81 (30 and 60 seconds) vs. *E. coli*, respectively. Accordingly, the present antibacterial compositions can be characterized as exhibiting

20 a log reduction of at least about 2 (after 30 seconds) or at least about 3 (after 60 seconds) vs. *S. aureus*, or of at least about 2.5 (after 30 seconds) or at least about 3.5 (after 60 seconds) vs. *E. coli*.

25 The antibacterial compositions of the present invention have several practical end uses, including hand cleansers, mouthwashes, surgical scrubs, body splashes, hand sanitizer gels, and similar personal care products. Additional types of

30 compositions include foamed compositions, such as creams, mousses, and the like, and compositions containing organic and inorganic filler materials, such as emulsions, lotions, creams, pastes, and the

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like. The compositions further can be used as an antibacterial cleanser for hard surfaces, for example, sinks and countertops in hospitals, food service areas, and meat processing plants. The present
5 antibacterial compositions can be manufactured as dilute ready-to-use compositions, or as concentrates that are diluted prior to use.

The compositions also can be incorporated into a web material to provide an antibacterial
10 wiping article. The wiping article can be used to clean and sanitize skin or inanimate surfaces.

The present antimicrobial compositions provide the advantages of a broad spectrum kill of Gram positive and Gram negative bacteria in short
15 contact times. The short contact time for a substantial log reduction of bacteria is important in view of the typical 15 to 60 second time frame used to cleanse and sanitize the skin and inanimate surfaces.

20 The present compositions are effective in short contact time because the antibacterial agent is present in the aqueous continuous phase of the composition, as opposed to surfactant micelles. The antibacterial agent, therefore, is available to
25 immediately begin reducing bacterial populations, and further is available to deposit on the skin to provide residual antibacterial efficacy. In addition, because the antibacterial agent is in solution as opposed to surfactant micelles, the absolute
30 amount of antimicrobial agent in the composition can be reduced without adversely affecting efficacy, and the antibacterial agent is not rinsed from the skin with the surfactant prior to performing its antibac-

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terial function. In addition, the amount of surfactant in the present antibacterial compositions typically is low, thereby providing additional environmental benefits.

5 The following examples illustrate various compositions of the present invention.

Example 20

Hand Wash Composition

10

A composition in accordance with the instant invention, suitable for use as a hand wash, was prepared. The composition contained the following components in the indicated weight percentages:

15

Ingredient	Weight Percent
Triclosan	0.3
Ammonium Lauryl Sulfate	0.75
Dipropylene Glycol	5.0
20 Sodium Xylene Sulfonate	10.0
Fragrance	0.05
Water	q.s.

25

The composition was prepared by admixing the dipropylene glycol, TCS, and fragrance until homogeneous (about 5 minutes). After the triclosan was completely dissolved, as evidenced by the absence of undissolved solid material, the sodium xylene sulfonate was added to the solution. The resulting mixture then was stirred to completely dissolve the sodium xylene sulfonate (about 5 minutes). Finally, the ammonium lauryl sulfate and

30

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water were added to the resulting solution, and the composition was stirred until homogeneous (about 5 minutes).

5 The composition had a weight ratio of
surfactant:triclosan of 2.5:1, and was at least
about 90% saturated with triclosan. The composition
was evaluated for antibacterial efficacy against *S.*
aureus and *E. coli* using a time kill test. Against
10 *S. aureus*, the composition exhibited a log reduction
of >4.07 in 30 seconds, while against *E. coli* the
composition exhibited a log reduction of 3.90 in 30
seconds. Thus, the composition exhibited an excel-
lent broad spectrum antibacterial activity. Also,
the composition was an excellent hand wash composi-
15 tion in an actual use test, providing both good
cleansing and a smooth feel to the hands.

Example 21

Body Splash Composition

20

A composition in accordance with the pres-
ent invention, suitable for use as a body splash, is
prepared using the following ingredients in the
following weight percentages:

25

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Ingredient	Weight Percent
Triclosan	0.3
Alkyl Polyglycoside	0.3
Propylene Glycol	14.4
Sodium Xylene Sulfonate	10.0
Ethanol	10.0
Fragrance	0.05
Water	q.s.

The composition is prepared by combining the triclosan, propylene glycol, fragrance, and ethanol, and admixing the components until all the triclosan is dissolved, as evidenced by the absence of undissolved solid material. The sodium xylene sulfonate then is added, and the resulting mixture is stirred until the sodium xylene sulfonate is completely dissolved. Finally, the alkyl polyglycoside and water are added, and the mixture again is stirred until homogeneous. The resulting composition forms an excellent and refreshing body splash that provides a desirable level of bacterial reduction on the skin of the user.

Example 22

Mouthwash Composition

A composition in accordance with the present invention, suitable for use as a mouthwash, is prepared using the following ingredients in the following weight percentages:

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Ingredient	Weight Percent
Triclosan	0.3
Alkyl Polyglycoside	0.3
Propylene Glycol	14.4
Sodium Xylene Sulfonate	10.0
Denatured alcohol	10.0
Oil of Wintergreen (flavor)	0.05
Water	q.s.

10

The composition is prepared by combining the triclosan, propylene glycol, flavor, and denatured alcohol, and admixing the components by any conventional means until all the triclosan is dissolved, as evidenced by the absence of undissolved solid material. Then, the sodium xylene sulfonate is added, and the resulting mixture is stirred until the sodium xylene sulfonate is completely dissolved. Finally, the alkyl polyglycoside and water are added, and the mixture again is stirred until homogeneous. The resulting composition forms an excellent and refreshing mouthwash that provides a desirable level of bacterial reduction on the teeth, gums, and tongue of the user.

25

Example 23

Wet Wipe Composition

30

A composition in accordance with the present invention, suitable for impregnating a nonwoven material for the preparation of a wet wipe article, was prepared using the following ingredients in the following weight percentages:

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5

Ingredient	Weight Percent
Triclosan	0.3
Ammonium Lauryl Sulfate	0.75
Dipropylene Glycol	5.0
Sodium Xylene Sulfonate	15.0
Water	q.s.

10

The composition was prepared by combining the triclosan and dipropylene glycol, and admixing the components until all the triclosan was dissolved, as evidenced by the absence of undissolved solid material. The sodium xylene sulfonate then was added, and the resulting mixture was stirred until the sodium xylene sulfonate was completely dissolved. Finally, the ammonium lauryl sulfate and water were added, and the mixture was again stirred until homogeneous.

20

25

A piece of nonwoven cellulosic web material (i.e., a commercial paper towel) then was dipped by hand into the composition to form a wet wipe article, suitable for wiping and cleaning surfaces, for example, hands. The article formed an excellent wet wipe and the impregnated antibacterial composition was freely expressed from the web to provide a broad spectrum antibacterial activity.

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Example 24Hand Wash Composition

A composition in accordance with the present invention, suitable for use as a hand wash, was prepared. The composition comprised the following components at the indicated weight percentages:

Ingredient	Weight Percent
Triclosan	0.3
Ammonium Lauryl Sulfate	0.75
Dipropylene Glycol	5.0
Sodium Xylene Sulfonate	15.0
Water	q.s.

The composition was prepared by first admixing the triclosan and dipropylene glycol until homogeneous (about 5 minutes). After the triclosan was completely dissolved, as evidenced by the absence of undissolved solid material, the sodium xylene sulfonate was added to the solution. The mixture then was stirred to completely dissolve the sodium xylene sulfonate (about 5 minutes). Finally, the ammonium lauryl sulfate and water were added to the resulting solution, and the composition was stirred until homogeneous (about 5 minutes).

The composition had a weight ratio of surfactant:triclosan of 2.5:1 and was at least about 90% saturated with triclosan. The composition was evaluated for its antibacterial efficacy against *S. aureus*, *E. coli*, *K. pneum.*, and *S. choler.* using a time kill test, and a contact time of 30 seconds.

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The composition exhibited log reductions of >3.59, >4.49, >3.20, and >4.27 against the four test organisms, respectively.

Thus, the composition exhibited an excellent broad spectrum antibacterial activity. In addition, the composition was an excellent hand wash composition in an actual use test, providing both good cleansing and a smooth feel to the hands.

Example 25

Comparison to a Previously Disclosed Composition

This example compares the antibacterial efficacy of a composition of the present invention to a previously disclosed composition. Accordingly, the composition of Example 24 was compared to the sole example disclosed in WO 98/01110. In both compositions, the active antibacterial agent was triclosan (TCS). Both compositions were evaluated for antibacterial efficacy in a time kill test against *S. aureus*, *E. coli*, *K. pneum.*, and *S. choler*. The example of WO 98/01110 was tested at 50% dilution, in accordance with the test procedure for viscous compositions. The following data summarizes the percent of active antibacterial agent in each composition at the test dilution (i.e., test dilution is 100% for the composition of Example 24 and 50% for the example of WO 98/01110), and the log reduction observed in the time kill test at a contact time of 30 seconds.

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Composition	% TCS	Log Reduction at 30 seconds			
		<i>S.</i> <i>aureus</i>	<i>E.</i> <i>coli</i>	<i>K.</i> <i>pneum.</i>	<i>S.</i> <i>choler</i>
Example 18	0.3	>4.60	>4.50	4.21	>4.68
WO 98/01110	0.5	3.29	0.29	1.00	0.45

10 This example demonstrates the superior
time kill performance of a composition of the pres-
ent invention compared to a prior composition, espe-
cially against Gram negative bacteria. This superi-
ority is demonstrated even through the comparative
15 composition contained substantially more active
antibacterial agent compared to the inventive compo-
sition. Thus, an inventive composition utilizes the
active agent more efficiently, as illustrated in a
higher log reduction using a reduced concentration
20 of antibacterial agent.

Example 26

Comparison to a Previously Disclosed Composition

25 This example compares the antibacterial
efficacy of a composition of the present invention
to a previously disclosed composition. Accordingly,
30 the composition of Example 24 was compared to a
composition disclosed in WO 96/06152. WO 96/06152
discloses effective compositions comprising TCS, an
anionic surfactant, a hydrotrope, a hydric solvent,
and further comprising an organic acid, specifically
35 citric acid. WO 96/06152 contains additional pH
adjusting agents, such as monoethanolamine and so-

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dium hydroxide. Further, the examples disclosed in WO 96/06152 all have a pH of 4 or 9.1, with no examples having a desirable, neutral pH of about 7. A pH of about 7 is desired for compositions contacting skin or inanimate surfaces because compositions of pH substantially different from 7, such as 4 or 9.1, have a greater potential to damage the surfaces they contact. Accordingly, the composition of Example 1 of WO 96/06152 (hereafter referred to as composition 26-A) was prepared. For comparison, composition 26-A was prepared as above, except that the pH was adjusted to 7 by the addition of further monoethanolamine (this composition hereafter referred to as composition 26-B). To provide an additional comparison, the composition of Example 3 of WO 96/06152 was prepared, except that it was prepared at a pH of 7 by the addition of further monoethanolamine (this composition is hereafter referred to as composition 26-C). The table below summarizes the results of a time kill test on the compositions of this example against the bacteria indicated at a contact time of 30 seconds.

Composition	pH	% TCS	Log Reduction at 30 Seconds			
			<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneum.</i>	<i>S. choler.</i>
Example 24	7.1	0.3	>4.54	>4.25	3.67	>4.77
Comparative 26-A	4	0.075	--	--	>4.84	--
Comparative 26-B	7	0.075	--	--	0.07	--
Comparative 26-C	7	0.15	4.44	2.91	0.28	4.67

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This example demonstrates the superior time kill performance of a composition of the present invention compared to prior compositions, especially with respect to Gram negative bacteria at a pH of about 7. From the data presented in this example, it can be concluded that the compositions of WO 96/06152 rely substantially on a relatively extreme pH (either 4 or 9, as disclosed) to achieve a desirable, rapid and broad spectrum reduction of bacterial populations. This is in contrast to Example 18 of the present invention, which provides a rapid broad spectrum bacteria kill at the desirable pH of about 7.

Example 27

Antibacterial Composition Containing PCMX

An antibacterial composition in accordance with the present invention containing p-chloro-m-xylenol (PCMX) as the active antibacterial agent was prepared. The composition contained the following components in the indicated weight percentages:

Ingredient	Weight Percent
PCMX	0.1
Ethanol	13.42
Water	q.s.

The composition was prepared by first mixing the PCMX and ethanol to completely solubilize the PCMX (about 5 minutes). After the PCMX was completely dissolved, as evidenced by the absence of

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undissolved solid material, the water was added, and the composition was stirred until homogeneous (about 5 minutes).

5 The composition was at least about 90% saturated with PCMX. The composition was evaluated for antibacterial efficacy against *S. aureus*, *E. coli*, *K. pneum.*, and *S. choler.* using a time kill test. Against *S. aureus*, the composition exhibited a log reduction of 4.16 in 30 seconds; against *E. coli* the composition exhibited a log reduction of >4.34 in 30 seconds; against *K. pneum.* the composition exhibited a log reduction of 3.99 in 30 seconds; and against *S. choler.* the composition exhibited a log reduction of >4.04 in 30 seconds. Thus, 10 the composition exhibited an excellent broad spectrum antibacterial activity. 15

Example 28

Antibacterial Composition Containing PCMX

20 A composition in accordance with the present invention incorporating p-chloro-m-xylene as the active antibacterial ingredient was prepared. The composition contained the following components in 25 the indicated weight percentages:

Ingredient	Weight Percent
PCMX	0.3
Ammonium Lauryl Sulfate	0.8
Water	q.s.

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The composition was prepared by first combining the PCMX and water, then adding the ammonium lauryl sulfate and mixing the components for such time as to completely admix the components and dissolve the PCMX (about 2 hours).

The composition was at least about 90% saturated with PCMX. The composition was evaluated for its antibacterial efficacy against *S. aureus* and *E. coli* using a time kill test. Against *S. aureus*, the composition exhibited a log reduction of >3.57 in 30 seconds; and against *E. coli* the composition exhibited a log reduction of >4.17 in 30 seconds. Thus, the composition exhibited an excellent broad spectrum antibacterial activity.

Obviously, many modifications and variations of the invention as hereinbefore set forth can be made without departing from the spirit and scope thereof, and, therefore, only such limitations should be imposed as are indicated by the appended claims.

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WHAT IS CLAIMED IS:

1. An antimicrobial composition comprising:

(a) about 0.001% to about 5%, by weight, of a phenolic antibacterial agent;

(b) about 0.1% to about 15%, by weight, of a surfactant selected from the group consisting of a C₈-C₁₈ alkyl sulfate, a C₈-C₁₈ fatty acid salt, a C₈-C₁₈ alkyl ether sulfate having one or two moles of ethoxylation, a C₈-C₁₈ alkamine oxide, a C₈-C₁₈ alkyl sarcosinate, a C₈-C₁₈ sulfoacetate, a C₈-C₁₈ sulfo-succinate, a C₈-C₁₈ alkyl diphenyl oxide disulfonate, a C₈-C₁₈ alkyl carbonate, a C₈-C₁₈ alpha-olefin sulfonate, a methyl ester sulfonate, and mixtures thereof; and

(c) water,

wherein the antibacterial agent is present in the composition in an amount of at least 50% of saturation concentration, when measured at room temperature.

2. The composition of claim 1 further comprising:

0% to about 25%, by weight, of a water-soluble hydric solvent, and

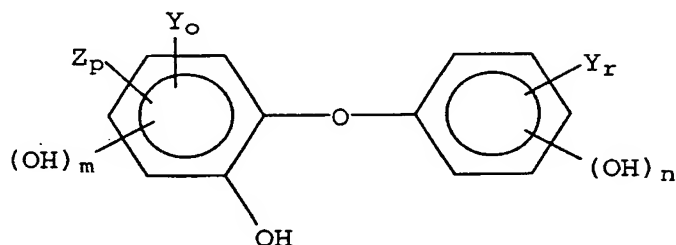
0% to about 30%, by weight, of a hydro-trope.

3. The composition of claim 1 comprising about 0.05% to about 2% by weight, of the phenolic antibacterial agent.

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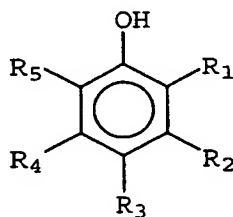
4. The composition of claim 1 wherein the phenolic antibacterial agent is selected from the group consisting of:

(a) a 2-hydroxydiphenyl compound having the structure



wherein Y is chlorine or bromine, Z is SO₂H, NO₂, or C₁-C₄ alkyl, r is 0 to 3, o is 0 to 3, p is 0 or 1, m is 0 or 1, and n is 0 or 1;

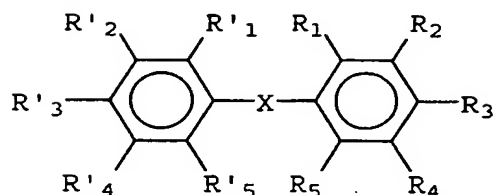
(b) a phenol derivative having the structure



wherein R₁ is hydro, hydroxy, C₁-C₄ alkyl, chloro, nitro, phenyl, or benzyl; R₂ is hydro, hydroxy, C₁-C₆ alkyl, or halo; R₃ is hydro, C₁-C₆ alkyl, hydroxy, chloro, nitro, or a sulfur in the form of an alkali metal salt or ammonium salt; R₄ is hydro or methyl, and R₅ is hydro or nitro;

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(c) a diphenyl compound having the structure



wherein X is sulfur or a methylene group, R_1 and R'_1 are hydroxy, and R_2 , R'_2 , R_3 , R'_3 , R_4 , R'_4 , R_5 , and R'_5 , independent of one another, are hydro or halo; and

(d) mixtures thereof.

5. The composition of claim 4 wherein the antibacterial agent comprises triclosan, p-chloro-m-xlenol, or mixtures thereof.

6. The composition of claim 1 wherein the surfactant is present in an amount of about 0.5% to about 10%, by weight of the composition.

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7. The composition of claim 1 wherein the surfactant is selected from the group consisting of a C₈-C₁₈ alkyl sulfate, a C₈-C₁₈ alkamine oxide, and mixtures thereof, and has a cation selected from the group consisting of sodium, ammonium, potassium, alkyl(C₁₋₄)ammonium, dialkyl(C₁₋₄)ammonium, trialkyl-(C₁₋₄)ammonium, alkanol(C₁₋₄)ammonium, dialkanol(C₁₋₄)-ammonium, trialkanol(C₁₋₄)ammonium, and mixtures thereof.

8. The composition of claim 1 wherein the surfactant comprises a lauryl sulfate, an octyl sulfate, a 2-ethylhexyl sulfate, lauramine oxide, and mixtures thereof.

9. The composition of claim 1 having a pH of about 5 to about 8.

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10. An antimicrobial composition comprising:

(a) about 0.001% to about 5%, by weight, of a phenolic antibacterial agent;

(b) about 0.1% to about 15%, by weight, of a surfactant selected from the group consisting of a C₈-C₁₈ alkyl sulfate, a C₈-C₁₈ fatty acid salt, a C₈-C₁₈ alkyl ether sulfate having one or two moles of ethoxylation, a C₈-C₁₈ alkamine oxide, a C₈-C₁₈ alkyl sarcosinate, a C₈-C₁₈ sulfoacetate, a C₈-C₁₈ sulfo-succinate, a C₈-C₁₈ alkyl diphenyl oxide disulfonate, a C₈-C₁₈ alkyl carbonate, a C₈-C₁₈ alpha-olefin sulfonate, a methyl ester sulfonate, and mixtures thereof; and

(c) water,

wherein the composition has a log reduction against Gram positive bacteria of at least 2 after 30 seconds of contact, as measured against *S. aureus*, and has a log reduction against Gram negative bacteria of at least 2.5 after 30 seconds of contact, as measured against *E. coli*.

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11. An antibacterial composition comprising:

(a) about 0.001% to about 5%, by weight, of a phenolic antimicrobial agent;

(b) about 0.1% to about 15%, by weight, of a surfactant selected from the group consisting of an anionic surfactant, a cationic surfactant, a nonionic surfactant, an ampholytic surfactant, and mixtures thereof;

(c) 0% to about 30%, by weight, of a hydrotrope;

(d) 0% to about 25%, by weight, of a water-soluble hydric solvent; and

(e) water,

wherein the composition contains at least one of the hydrotrope and hydric solvent

and wherein the antimicrobial agent is present in an amount of at least 25% of saturation concentration, when measured at room temperature.

12. The composition of claim 11 wherein the antibacterial agent is present in an amount of at least 50% of saturation concentration.

13. The composition of claim 11 wherein the antibacterial agent is present in an amount of at least 75% of saturation concentration.

14. The composition of claim 11 wherein the antibacterial agent is present in an amount of at least 95% of saturation concentration.

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15. The composition of claim 11 wherein the surfactant comprises an anionic surfactant, an ampholytic surfactant, or a mixture thereof.

16. The composition of claim 11 comprising a hydrotrope and a hydric solvent.

17. The composition of claim 11 wherein the hydrotrope is present in an amount of about 5% to about 20% by weight.

18. The composition of claim 11 wherein the hydric solvent present in an amount of about 5% to about 15% by weight.

19. The composition of claim 11 wherein the hydric solvent comprises an alcohol, a diol, a triol, and mixtures thereof.

20. The composition of claim 11 wherein the hydric solvent comprises methanol, ethanol, isopropyl alcohol, n-butanol, n-propyl alcohol, ethylene glycol, propylene glycol, glycerol, diethylene glycol, dipropylene glycol, tripropylene glycol, hexylene glycol, butylene glycol, 1,2,6-hexanetriol, sorbitol, PEG-4, or mixtures thereof.

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21. The composition of claim 11 wherein the hydrotrope is selected from the group consisting of sodium cumene sulfonate, ammonium cumene sulfonate, ammonium xylene sulfonate, potassium toluene sulfonate, sodium toluene sulfonate, sodium xylene sulfonate, toluene sulfonic acid, xylene sulfonic acid, sodium polynaphthalene sulfonate, sodium polystyrene sulfonate, sodium methyl naphthalene sulfonate, disodium succinate, and mixtures thereof.

22. The composition of claim 11 having a pH of about 5 to about 8.

23. The composition of claim 11 comprising:

(a) about 0.01% to about 0.5%, by weight, of the antimicrobial agent;

(b) about 0.1% to about 5%, by weight, of the surfactant;

(c) about 5% to about 20%, by weight, of the hydrotrope; and

(d) about 2% to about 15%, by weight, of the hydric solvent.

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24. An antibacterial composition comprising:

(a) about 0.001% to about 5%, by weight, of a phenolic antimicrobial agent;

(b) about 0.1% to about 15%, by weight, of a surfactant selected from the group consisting of an anionic surfactant, a cationic surfactant, a nonionic surfactant, an ampholytic surfactant, and mixtures thereof;

(c) about 0% to about 30%, by weight, of a hydrotrope;

(d) about 0% to about 25%, by weight, of a water-soluble hydric solvent; and

(e) water,

wherein the composition contains at least one of the hydrotrope and hydric solvent,

and wherein the composition has a log reduction against Gram positive bacteria of at least 2 after 30 seconds of contact, as measured against *S. aureus*, and has a log reduction against Gram negative bacteria of at least 2.5 after 30 seconds of contact, as measured against *E. coli*.

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25. An antibacterial composition comprising:

(a) about 0.001% to about 5%, by weight, of a phenolic antimicrobial agent;

(b) 0% to about 40%, by weight, of a hydrotrope;

(c) 0% to about 60%, by weight, of a water-soluble hydric solvent; and

(d) water,

wherein the composition contains at least one of the hydrotrope and hydric solvent,

and wherein the antimicrobial agent is present in an amount of at least 25% of saturation concentration, when measured at room temperature.

26. The composition of claim 25 further comprising 0% to about 10%, by weight, of a surfactant selected from the group consisting of an anionic surfactant, a cationic surfactant, a nonionic surfactant, an ampholytic surfactant, and mixtures thereof.

27. The composition of claim 25 comprising a hydrotrope and a hydric solvent.

28. The composition of claims 1, 11, and 25 having a log reduction against Gram positive bacteria of at least 2 after 30 seconds of contact, as measured against *S. aureus*, and a log reduction against Gram negative bacteria of at least 2.5 after 30 seconds of contact, as measured against *E. coli*.

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29. The composition of claims 11 and 25 wherein the antibacterial agent is present in an amount of at least 50% of saturation concentration.

30. The composition of claims 1, 11, and 25 wherein the antibacterial agent is present in an amount of at least 75% of saturation concentration.

31. The composition of claims 1, 11, and 25 wherein the antibacterial agent is present in an amount of at least 95% of saturation concentration.

32. An antibacterial composition comprising:

(a) about 0.001% to about 5%, by weight, of a phenolic antimicrobial agent;

(b) 0% to about 40%, by weight, of a hydrotrope;

(c) 0% to about 60%, by weight, of a water-soluble hydric solvent; and

(d) water,

wherein the composition contains at least one of the hydrotrope and hydric solvent,

and wherein the composition has a log reduction against Gram positive bacteria of at least 2 after 30 seconds of contact, as measured against *S. aureus*, and has a log reduction against Gram negative bacteria of at least 2.5 after 30 seconds of contact, as measured against *E. coli*.

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33. A method of reducing a bacteria population on a surface comprising contacting the surface with a composition of claim 1 for 30 seconds to achieve a log reduction of at least 2 against *S. aureus* and at least 2.5 against *E. coli*, then rinsing the composition from the surface.

34. The method of claim 33 wherein the surface is a skin of a mammal.

35. The method of claim 33 wherein the surface is a hard, inanimate surface.

36. A method of reducing a bacteria population on a surface comprising contacting the surface with a composition of claim 11 for 30 seconds to achieve a log reduction of at least 2 against *S. aureus* and at least 2.5 against *E. coli*, then rinsing the composition from the surface.

37. A method of reducing a bacteria population on a surface comprising contacting the surface with a composition of claim 25 for 30 seconds to achieve a log reduction of at least 2 against *S. aureus* and at least 2.5 against *E. coli*, then rinsing the composition from the surface.

38. The method of claims 35 through 37 wherein the composition contacts the surface for 60 seconds to achieve a log reduction of at least 3 against *S. aureus*.

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39. The method of claims 35 through 37 wherein the composition contacts the surface for 60 seconds to achieve a log reduction of at least 3.75 against *E. coli*.

40. The method of claims 36 and 37 wherein the composition contacts the surface for 30 seconds to achieve a log reduction of at least 2 against *K. pneum.*

41. An antimicrobial composition comprising:

- (a) about 0.05% to about 5%, by weight, of a phenolic antibacterial agent;
- (b) about 1% to about 40%, by weight, of a disinfecting alcohol;
- (c) about 0.1% to about 5%, by weight, of a gelling agent; and
- (d) water,

wherein the composition is free of a surfactant,

and wherein the antibacterial agent is present in the composition in an amount of at least 50% of saturation concentration, when measured at room temperature.

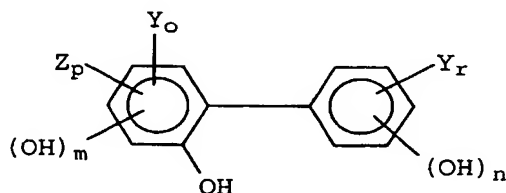
42. The composition of claim 41 comprising about 0.1% to about 4% by weight, of the phenolic antibacterial agent.

43. The composition of claim 41 comprising about 0.25% to about 2% by weight, of the phenolic antibacterial agent.

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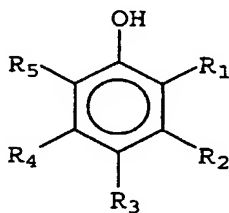
44. The composition of claim 41 wherein the phenolic antibacterial agent is selected from the group consisting of:

(a) a 2-hydroxydiphenyl compound having the structure



wherein Y is chlorine or bromine, Z is SO₂H, NO₂, or C₁-C₄ alkyl, r is 0 to 3, o is 0 to 3, p is 0 or 1, m is 0 or 1, and n is 0 or 1;

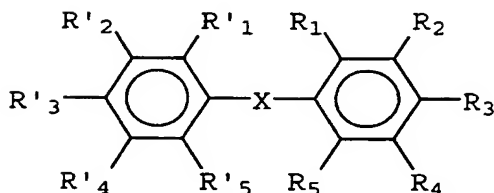
(b) a phenol derivative having the structure



wherein R₁ is hydro, hydroxy, C₁-C₄ alkyl, chloro, nitro, phenyl, or benzyl; R₂ is hydro, hydroxy, C₁-C₆ alkyl, or halo; R₃ is hydro, C₁-C₆ alkyl, hydroxy, chloro, nitro, or a sulfur in the form of an alkali metal salt or ammonium salt; R₄ is hydro or methyl, and R₅ is hydro or nitro;

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(c) a diphenyl compound having the structure



wherein X is sulfur or a methylene group, R_1 and R'_1 are hydroxy, and R_2 , R'_2 , R_3 , R'_3 , R_4 , R'_4 , R_5 , and R'_5 , independent of one another, are hydro or halo; and

(d) mixtures thereof.

45. The composition of claim 44 wherein the antibacterial agent comprises triclosan, p-chloro-m-xyleneol, or mixtures thereof.

46. The composition of claim 41 wherein the disinfecting alcohol is present in an amount of about 2% to about 35%, by weight.

47. The composition of claim 41 wherein the disinfecting alcohol is present in an amount of about 5% to about 30%, by weight.

48. The composition of claim 41 wherein the disinfecting alcohol is a C_{1-6} alcohol or mixtures thereof.

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49. The composition of claim 41 wherein the disinfecting alcohol is selected from the group consisting of methanol, ethanol, isopropyl alcohol, n-butanol, n-propyl alcohol, and mixtures thereof.

50. The composition of claim 41 wherein the gelling agent is present in an amount of about 0.1% to about 3%, by weight.

51. The composition of claim 41 wherein the gelling agent is present in an amount of about 0.25% to about 2.5%, by weight.

52. The composition of claim 41 wherein the gelling agent comprises a natural gum, a synthetic polymer, a clay, an oil, a wax, and mixtures thereof.

53. The composition of claim 41 wherein the gelling agent is selected from the group consisting of an acrylate homopolymer, an acrylate copolymer, a carbomer, a polyacrylic acid, cellulose, a cellulose derivative, guar, a guar derivative, algin, an algin derivative, a water-insoluble C₈-C₂₀ alcohol, carrageenan, and mixtures thereof.

54. The composition of claim 41 wherein the gelling agent comprises a polyacrylic acid, a polyacrylate, a smectite clay, or a polyquaternium compound.

55. The composition of claim 41 having a pH of about 5 to about 8.

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56. An antimicrobial composition comprising:

- (a) about 0.05% to about 5%, by weight, of a phenolic antibacterial agent;
- (b) about 1% to about 40%, by weight, of a disinfecting alcohol;
- (c) about 0.1% to about 5%, by weight, of a gelling agent; and
- (d) water,

wherein the composition is free of a surfactant,

and wherein the composition has a log reduction against Gram positive bacteria of at least 2 after 30 seconds of contact, as measured against *S. aureus*, or has a log reduction against Gram negative bacteria of at least 2.5 after 30 seconds of contact, as measured against *E. coli*.

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57. An antibacterial composition comprising:

- (a) about 0.05% to about 5%, by weight, of a phenolic antimicrobial agent;
- (b) about 1% to about 40%, by weight, of a disinfecting alcohol;
- (c) about 0.1% to about 5%, by weight, of a gelling agent;
- (d) 0.1% to about 30%, by weight, of a hydrotrope;
- (e) water,

wherein the composition is free of a surfactant,

and wherein the antimicrobial agent is present in an amount of at least 25% of saturation concentration, when measured at room temperature.

58. The composition of claim 57 wherein the antibacterial agent is present in an amount of at least 50% of saturation concentration.

59. The composition of claim 57 wherein the hydrotrope is present in an amount of about 0.5% to about 25% by weight.

60. The composition of claim 57 wherein the gelling agent comprises a natural gum, a synthetic polymer, a clay, an oil, a wax, and mixtures thereof.

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61. The composition of claim 57 further comprising about 0.1% to about 50%, by weight, of a polyhydric solvent selected from the group consisting of a diol, a triol, and mixtures thereof.

62. The composition of claim 61 wherein the polyhydric solvent comprises ethylene glycol, propylene glycol, glycerol, diethylene glycol, dipropylene glycol, tripropylene glycol, hexylene glycol, butylene glycol, 1,2,6-hexanetriol, sorbitol, PEG-4, or mixtures thereof.

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63. The composition of claim 57 wherein the hydrotrope is selected from the group consisting of sodium cumene sulfonate, ammonium cumene sulfonate, ammonium xylene sulfonate, potassium toluene sulfonate, sodium toluene sulfonate, sodium xylene sulfonate, toluene sulfonic acid, xylene sulfonic acid, sodium polynaphthalene sulfonate, sodium polystyrene sulfonate, sodium methyl naphthalene sulfonate, disodium succinate, and mixtures thereof.

64. The composition of claim 57 having a pH of about 5 to about 8.

65. The composition of claim 57 comprising:

- (a) about 0.25% to about 2%, by weight, of the antimicrobial agent;
- (b) about 5% to about 30%, by weight, of a disinfecting alcohol;
- (c) about 0.25% to about 2.5%, by weight, of the gelling agent; and
- (d) about 1% to about 20%, by weight, of the hydrotrope.

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66. An antibacterial composition comprising:

- (a) about 0.05% to about 5%, by weight, of a phenolic antimicrobial agent;
- (b) about 1% to about 40%, by weight, of a disinfecting alcohol;
- (c) about 0.1% to about 5%, by weight, of a gelling agent;
- (d) 0.1% to about 30%, by weight, of a hydrotrope;
- (e) water,

wherein the composition is free of a surfactant,

and wherein the composition has a log reduction against Gram positive bacteria of at least 2 after 30 seconds of contact, as measured against *S. aureus*, or has a log reduction against Gram negative bacteria of at least 2.5 after 30 seconds of contact, as measured against *E. coli*.

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67. An antibacterial composition comprising:

- (a) about 0.05% to about 5%, by weight, of a phenolic antimicrobial agent;
- (b) about 1% to about 40%, by weight, of a disinfecting alcohol;
- (c) about 0.1% to about 30%, by weight, of a hydrotrope; and
- (d) water,

wherein the composition is free of a surfactant,

and wherein the antimicrobial agent is present in an amount of at least 25% of saturation concentration, when measured at room temperature.

68. The composition of claims 41, 57, and 67 having a log reduction against Gram positive bacteria of at least 2 after 30 seconds of contact, as measured against *S. aureus*, and a log reduction against Gram negative bacteria of at least 2.5 after 30 seconds of contact, as measured against *E. coli*.

69. The composition of claims 41, 57, and 67 wherein the antibacterial agent is present in an amount of at least 75% of saturation concentration.

70. The composition of claims 41, 57, and 67 wherein the antibacterial agent is present in an amount of at least 95% of saturation concentration.

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71. An antibacterial composition comprising:

- (a) about 0.05% to about 5%, by weight, of a phenolic antimicrobial agent;
- (b) about 1% to about 40%, by weight, of a disinfecting alcohol;
- (c) about 0.1% to about 30%, by weight, of a hydrotrope; and
- (d) water,

wherein the composition is free of a surfactant,

and wherein the composition has a log reduction against Gram positive bacteria of at least 2 after 30 seconds of contact, as measured against *S. aureus*, or has a log reduction against Gram negative bacteria of at least 2.5 after 30 seconds of contact, as measured against *E. coli*.

72. A method of reducing a bacteria population on a surface comprising contacting the surface with a composition of claim 41 for a sufficient time to provide a log reduction of bacteria of at least 2 against *S. aureus* and at least 2.5 against *E. coli*, then rinsing the composition from the surface.

73. The method of claim 72 wherein the surface is a skin of a mammal.

74. The method of claim 72 wherein the surface is a hard, inanimate surface.

75. A method of reducing a bacteria population on a surface comprising contacting the surface with a composition of claim 57 for a sufficient time to provide a log reduction of bacteria of at least 2 against *S. aureus* and at least 2.5 against *E. coli*, then rinsing the composition from the surface.

76. A method of reducing a bacteria population on a surface comprising contacting the surface with a composition of claim 67 for a sufficient time to provide a log reduction of bacteria of at least 2 against *S. aureus* and at least 2.5 against *E. coli*, then rinsing the composition from the surface.

77. The method of claims 72, 75, and 76 wherein the composition contacts the surface for 30 seconds to achieve a log reduction of at least 2 against *S. aureus*.

78. The method of claims 72, 75, and 76 wherein the composition contacts the surface for 60 seconds to achieve a log reduction of at least 3 against *S. aureus*.

79. The method of claims 72, 75, and 76 wherein the composition contacts the surface for 30 seconds to achieve a log reduction of at least 2.5 against *E. coli*.

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80. The method of claims 72, 75, and 76 wherein the composition contacts the surface for 60 seconds to achieve a log reduction of at least 3.75 against *E. coli*.

81. The method of claims 75 and 76 wherein the composition contacts the surface for 30 seconds to achieve a log reduction of at least 2 against *K. pneum.*

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WO 00/78275 A3

(54) Title: ANTIBACTERIAL COMPOSITIONS

(57) Abstract: Antibacterial compositions having enhanced antibacterial effectiveness are disclosed. The antibacterial compositions contain a phenolic antibacterial agent, a surfactant or a disinfecting alcohol, and water, wherein a percent saturation of the antibacterial agent in a continuous aqueous phase of the composition is at least 25 %.

INTERNATIONAL SEARCH REPORT

Internal Application No
PCT/US 00/15729

A. CLASSIFICATION OF SUBJECT MATTER

IPC 7 A01N31/16 A01N25/30 A01N25/04 A01N25/02 C11D3/60
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According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A01N

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

EPO-Internal, WPI Data, PAJ, CHEM ABS Data

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 46218 A (CIBA GEIGY AG ;SCHNYDER MARCEL (CH); OCHS DIETMAR (DE)) 11 December 1997 (1997-12-11)	1-40
X	the whole document	24-32, 37-40
X	WO 96 06152 A (MOLDOVANYI LASZLO ;CIBA GEIGY AG (CH)) 29 February 1996 (1996-02-29)	1-40
X	cited in the application the whole document	24-32, 37-40

☒ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

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INTERNATIONAL SEARCH REPORT

Inter. Application No
PCT/US 00/15729

C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT		
Category	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	GB 743 984 A (MONSANTO CHEMICALS LIMITED) 25 January 1956 (1956-01-25) page 1, line 9 -page 2, line 65; claims; examples	1-8, 10-15, 18-20, 24-26, 28-40
X	US 3 326 808 A (M.M.NOSEWORTHY) 20 June 1967 (1967-06-20) column 1, line 16 -column 2, line 32; example I	1-15, 17-20, 22, 24-26, 28-40
X	US 5 635 462 A (FENDLER ELEANOR J ET AL) 3 June 1997 (1997-06-03) column 1, line 64 -column 5, line 15 column 6, line 60 -column 7, line 4	1-15, 17-20, 22, 24-26, 28-40
X	column 7, line 23 - line 32; claims column 2, line 62 -column 3, line 29	24-26, 28-32, 37-40
A		41-81
X	CHEMICAL ABSTRACTS, vol. 122, no. 2, 9 January 1995 (1995-01-09) Columbus, Ohio, US; abstract no. 16825, KJAERHEIM, V. ET AL: "Biological activities of different triclosan-detergent combinations" XP002150726	1-10, 33-35
A	abstract & COLLOIDS SURF., B (1994), 3(1/2), 19-24 , 1994,	41-81
A	DE 195 30 833 A (CIBA GEIGY AG) 29 February 1996 (1996-02-29)	1-40
A	page 2 -page 5, line 43; claims; examples 1,3,5,7	41-81
X	EP 0 259 249 A (CIBA GEIGY AG) 9 March 1988 (1988-03-09) page 2 -page 4, line 12; examples	24-32, 37-40
Y	page 6, line 20 - line 21; example 26	45, 57-67, 71,76

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INTERNATIONAL SEARCH REPORT

Int. .ional Application No

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C.(Continuation) DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	<p>DATABASE WPI Section Ch, Week 198946 Derwent Publications Ltd., London, GB; Class D21, AN 1989-292819 XP002164623 -& JP 01 249897 A (CIBA GEIGY AG), 5 October 1989 (1989-10-05) abstract & AU 30018 89 A (CIBA-GEIGY) 17 August 1989 (1989-08-17)</p>	<p>24-32, 37-40</p>
X	<p>EP 0 855 440 A (PROCTER & GAMBLE) 29 July 1998 (1998-07-29) page 2, line 20 - line 31 page 5, line 34 - line 40 page 5, line 55 -page 6, line 23 page 9, line 3 - line 16; examples 2,4,6,7</p>	<p>24-32, 37-40</p>
X	<p>EP 0 505 935 A (BECTON DICKINSON CO) 30 September 1992 (1992-09-30) cited in the application page 3, last line -page 4, line 37 page 6, line 16 - line 31; example 1</p>	<p>24-26, 28-32, 37-40</p>
X	<p>WO 95 09605 A (HENKEL CORP) 13 April 1995 (1995-04-13) cited in the application page 2, line 15 -page 4; examples 1,3</p>	<p>24-26, 28-32, 37-40</p>
X	<p>EP 0 604 848 A (TOKO YAKUHHIN KOGYO KK) 6 July 1994 (1994-07-06) cited in the application</p>	<p>24-26, 28-32, 37-44, 46-53, 55,56, 68-70, 72,73, 75,77-81</p>
Y	<p>page 3, line 21 -page 4, line 17; claims; example 15</p>	<p>45, 57-67, 71,76</p>
X	<p>US 5 288 486 A (WHITE JOHN H) 22 February 1994 (1994-02-22) column 1, line 31 -column 2</p>	<p>41-56, 68-70, 72,73, 75,77-81</p>
A	<p>US 5 403 864 A (BRUCH MARY RUTH K ET AL) 4 April 1995 (1995-04-04) column 1, line 60 -column 2, line 52 claims</p>	<p>41-81</p>
A	<p>FR 2 629 095 A (RECKITT COLMAN) 29 September 1989 (1989-09-29) page 1; claims</p>	<p>41-81</p>

INTERNATIONAL SEARCH REPORT

International application No.
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Box I Observations where certain claims were found unsearchable (Continuation of item 1 of first sheet)

This International Search Report has not been established in respect of certain claims under Article 17(2)(a) for the following reasons:

1. ☐ Claims Nos.:
because they relate to subject matter not required to be searched by this Authority, namely:
2. ☐ Claims Nos.:
because they relate to parts of the International Application that do not comply with the prescribed requirements to such an extent that no meaningful International Search can be carried out, specifically:
3. ☐ Claims Nos.:
because they are dependent claims and are not drafted in accordance with the second and third sentences of Rule 6.4(a).

Box II Observations where unity of invention is lacking (Continuation of item 2 of first sheet)

This International Searching Authority found multiple inventions in this international application, as follows:

see additional sheet

1. ☒ As all required additional search fees were timely paid by the applicant, this International Search Report covers all searchable claims.
2. ☐ As all searchable claims could be searched without effort justifying an additional fee, this Authority did not invite payment of any additional fee.
3. ☐ As only some of the required additional search fees were timely paid by the applicant, this International Search Report covers only those claims for which fees were paid, specifically claims Nos.:
4. ☐ No required additional search fees were timely paid by the applicant. Consequently, this International Search Report is restricted to the invention first mentioned in the claims; it is covered by claims Nos.:

Remark on Protest

- ☐ The additional search fees were accompanied by the applicant's protest.
- ☒ No protest accompanied the payment of additional search fees.

FURTHER INFORMATION CONTINUED FROM PCT/ISA/ 210

This International Searching Authority found multiple (groups of) inventions in this international application, as follows:

1. Claims: 1-23, 33-36 (all completely), 24-32, 37-40 (all partially)

An antimicrobial composition comprising
(a) 0.001-5% by weight of a phenolic antibacterial agent;
(b) 0.1% -15% by weight of a surfactant selected from the group specified in independent claim 1; and
(c) water;
and corresponding methods of reducing bacteria populations using the composition

2. Claims: 24-32, 37-40 (all partially)

An antimicrobial composition comprising
(a) 0.001-5% by weight of a phenolic antibacterial agent;
(b) 0-40% of a hydrotrope;
(c) 0-60% of a water-soluble hydric solvent and
(d) water;
with provision that at least one of components (b) and (c) is present;
and corresponding methods of reducing bacteria populations using the composition

3. Claims: 41-81 (all completely), 24-32, 37-40 (all partially)

An antimicrobial composition comprising
(a) 0.05-5% by weight of a phenolic antibacterial agent;
(b) 1-40% of a disinfecting alcohol; and
(c) water;
with the provision that the composition is free of a surfactant,
and corresponding methods of reducing bacteria populations using the composition

INTERNATIONAL SEARCH REPORT

International Application No

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Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9746218 A	11-12-1997	AU 2959497 A BR 9709422 A CA 2252555 A CN 1220597 A EP 0914085 A JP 2000512276 T	05-01-1998 10-08-1999 11-12-1997 23-06-1999 12-05-1999 19-09-2000
WO 9606152 A	29-02-1996	AU 3345195 A BG 101306 A BR 9508767 A CZ 9700555 A EP 0777716 A FI 970741 A HU 77706 A JP 10504591 T SK 24597 A	14-03-1996 30-09-1997 11-11-1997 11-06-1997 11-06-1997 21-02-1997 28-07-1998 06-05-1998 06-08-1997
GB 743984 A	25-01-1956	FR 1090033 A	25-03-1955
US 3326808 A	20-06-1967	GB 1076343 A	19-07-1967
US 5635462 A	03-06-1997	NONE	
DE 19530833 A	29-02-1996	NONE	
EP 0259249 A	09-03-1988	AU 7599987 A BR 8703830 A DK 382787 A JP 63045217 A NO 873080 A	28-01-1988 29-03-1988 24-01-1988 26-02-1988 25-01-1988
JP 1249897 A	05-10-1989	AU 3001889 A BR 8900685 A	17-08-1989 10-10-1989
EP 0855440 A	29-07-1998	EP 0855439 A AU 5917198 A BR 9807005 A CN 1255156 T EP 0971995 A HU 0001655 A PL 336995 A WO 9832821 A US 6152152 A	29-07-1998 18-08-1998 14-03-2000 31-05-2000 19-01-2000 28-09-2000 31-07-2000 30-07-1998 28-11-2000
EP 0505935 A	30-09-1992	AT 163039 T AU 653200 B AU 1100192 A CA 2061009 A,C DE 69224312 D DE 69224312 T DK 505935 T ES 2111578 T JP 1987120 C JP 5097602 A JP 7023286 B NO 180089 B NZ 241579 A US 5439681 A	15-02-1998 22-09-1994 01-10-1992 26-09-1992 12-03-1998 28-05-1998 23-09-1998 16-03-1998 08-11-1995 20-04-1993 15-03-1995 04-11-1996 27-04-1994 08-08-1995

INTERNATIONAL SEARCH REPORT

International Application No

PCT/US 00/15729

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
WO 9509605 A	13-04-1995	AU 7920394 A EP 0739196 A	01-05-1995 30-10-1996
EP 0604848 A	06-07-1994	JP 2533723 B JP 6199700 A AT 185836 T CA 2111932 A,C CN 1090126 A,B DE 69326824 D DE 69326824 T DK 604848 T ES 2139622 T GR 3031577 T US 5750579 A	11-09-1996 19-07-1994 15-11-1999 29-06-1994 03-08-1994 25-11-1999 27-01-2000 17-04-2000 16-02-2000 31-01-2000 12-05-1998
US 5288486 A	22-02-1994	AT 63670 T CA 1299098 A DE 3679383 D EP 0223681 A JP 1981878 C JP 7010770 B JP 62106012 A	15-06-1991 21-04-1992 27-06-1991 27-05-1987 25-10-1995 08-02-1995 16-05-1987
US 5403864 A	04-04-1995	NONE	
FR 2629095 A	29-09-1989	NONE	

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